UNIVERSITY OF LONDON THESIS

Degree PhD Year 2006 Name of Author THOMASSON Rachel

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Visual Cognition after Hemispherectomy: A Neuropsychological Study

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Thesis submitted for examination for the Ph.D degree of the University of London

March, 2006

Abstract

The detrimental effects of medically intractable seizures on the developing brain have been previously documented, and a wealth of literature provides support for surgical intervention. The removal of a cerebral hemisphere (hemispherectomy) may be considered the most radical of these interventions, yet there is often no further detriment to general intellectual function or language after surgery. The aims of these studies were to evaluate visual cognitive abilities after hemispherectomy for intractable childhood epilepsy, to establish whether any differences were apparent between patients according to side of hemispheric removal, and to determine the relationship between age at seizure onset and subsequent cognitive outcome. Twenty two (12 left, 10 right) hemispherectomised patients took part in these studies. The possibility of dissociation between general intelligence levels and visual cognitive ability in the lone hemisphere was addressed by using control participants (n = 19) matched to individual patients according to chronological age, gender and general non-verbal reasoning ability.

Neuropsychological and experimental measurements were used to assess visual cognitive functions including stereopsis, visual attention, face processing, spatial abilities and construction. Impaired performance, particularly on more complex tasks was found in all groups, and was consistent with generic reduction of cognitive function. These difficulties occurred regardless of side of injury, though visual recall and recognition may be selectively disadvantaged in the lone left hemisphere and warrants further study. Hemispherectomised patients and their controls differed on measures of visual search and memory for complex designs, suggesting some limitations of function in the lone hemisphere may occur above and beyond generalised reduction of cognitive function.

Results were broadly consistent with theories of equipotentiality and interactive specialisation, whereby the unfolding of a hemisphere specific architectural blueprint is disrupted by cerebral injury, enabling a range of functions to develop in either hemisphere, albeit with limitations that appear to be a product of generic reduction in cognitive function and lack of processing space.

Acknowledgements

I would like to thank my supervisors Professor Faraneh Vargha-Khadem and Dr Michelle de Haan, for providing the opportunity to undertake this research and to learn more about this unique, inspiring and wonderful group of patients. I am very grateful to them for their support, wisdom and guidance throughout the thesis whilst allowing valuable latitude in which to gain a sense of independence and responsibility with respect to constructing, running and reporting a research project of this nature. Their advice throughout the final stages was insightful, encouraging and constructive, enabling each draft of the thesis to improve further, in addition to enhancing my creative and critical faculties even in the most challenging moments.

I was very fortunate to work within an institute that is a multidisciplinary centre of excellence for child health. As a result, I had contact with many experts in their fields, who were very generous with their time and offered priceless advice throughout the thesis. A very special thank you to Dr Frederique Liegeois who taught me so much about the rudiments of running a research project, from patient recruitment and data collection to analysis and presentation. Her time, patience and wisdom were always given generously and I am especially grateful. I would like to thank Brian Neville and Helen Cross for sharing their expertise on childhood epilepsy and hemispherectomy. I am also very grateful to Professor Charles Polkey, for his time and expertise regarding the surgical procedures of hemispherectomy and his knowledge of the Kings College Hospital patient group. Professor Heidi Feldman provided generous amounts of time to discuss construction of testing protocols and to review strategies for data analysis. Regarding the latter, I am extremely grateful to Dr de Haan and Dr Martin King for devoting time, consideration and patience to supervising statistical analyses for this study. A big thank you also to everyone at the Wolfson centre. Fellow Ph.D students Alison, Anna, Leasha, Emma, Alex and Briony were wonderfully supportive, and departmental administrator Serife Dervish was brilliantly organised. A special thanks to treasured friend and graphic designer Alison Menzies for formatting advice. Finally I would like to thank the children and families that took part in this research, without whom, this thesis would not have existed. Their commitment and enthusiasm for the project was truly inspiring and has cemented an aspiration to continue what I have started, namely a fascinating avenue of enquiry that will always have a place in my daily thoughts as a paediatric neurologist.

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1 Introduction

This thesis reports the results of neuropsychological investigations of children and young adults that have undergone hemispherectomy for intractable seizures, with a view to gaining an understanding of the integrity of visual cognition in these patients. Although language function after hemispherectomy is well documented, relatively little is known about visual cognitive function after this procedure. Studies of neurologically intact adults and patients with focal unilateral cerebral lesions provide support for the concept of functional lateralisation of visual cognition, with left and right hemispheres demonstrating different functional profiles. Debate exists as to whether the concept of lateralisation of function applies to the developing brain, with three principal schools of thought representing the spectrum of beliefs surrounding these issues. The equipotentiality hypothesis suggests that the hemispheres are equipotent at birth and remain so until later in childhood. In contrast, the early specialisation hypothesis states that hemispheric specialisation exists at birth. Ontogenic or interactive specialisation hypotheses represent an intermediate point of view whereby early hemispheric specialisation may be curtailed by the presence of injury due to the plasticity of the developing brain. As development proceeds, the inherent functional specialisation of each hemisphere becomes manifest and thus reorganisation of function becomes less likely.

The purpose of this thesis is to characterize the nature and extent of visual cognitive impairment after hemispherectomy, and to investigate possible differences in function between the isolated left and right hemisphere. Furthermore, use of control subjects enabled consideration of the effects of a generic reduction in cognitive function in an attempt to identify difficulties specifically associated with cognising with one functional hemisphere.

This chapter is divided into five sections. The first section is concerned with the structural and functional anatomy of the visual system. It is necessary to consider the anatomy of the visual system to comprehend the breadth and complexity of the neural substrates subserving visual cognitive function, and to appreciate the magnitude of possible functional loss after removing a cerebral hemisphere. Pre geniculate anatomy is also included as retrograde degeneration is apparent following hemispherectomy. The second section is focused on the development of the visual system, to demonstrate the gradual increase in sophistication of perceptual and cognitive functions. The third section is focused on the debate surrounding laterality of visual cognitive functions, to provide an overview of the principal contributions of the left and right cerebral hemispheres to visual cognitive function in adults and children. The fourth section examines the interface between sections two and three via discussion of conceptual models of plasticity and reorganisation of cognitive functions following unilateral cerebral injury. Hemispherectomy is then considered in section five as a model to investigate these issues. The intractable epilepsy syndromes leading to hemispherectomy are described to give an overview of types of cerebral pathology encountered in the hemispherectomised cases. The surgical procedures for hemispherectomy are then outlined followed by a review of outcome studies that focus on clinical and neuropsychological outcome in children and adults.

1.1 Anatomy of the visual system

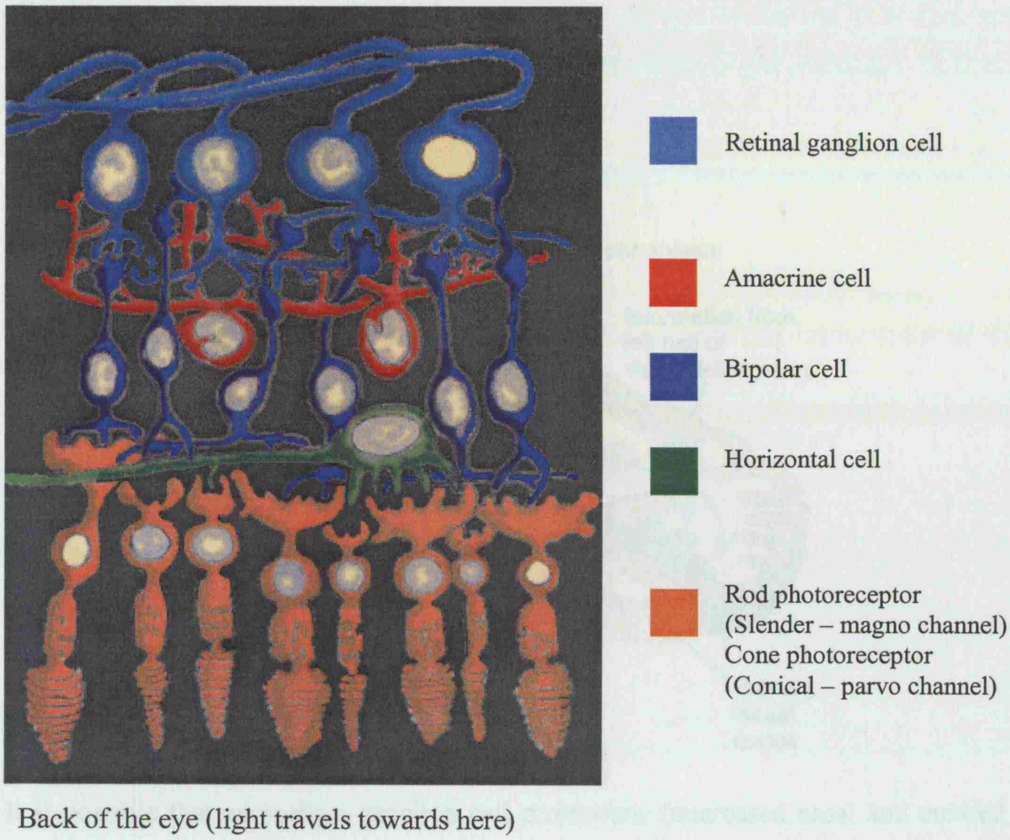
The human visual system is often conceptualised as a collection of parallel processing streams, enriched by feedforward, feedback and horizontal connectivity. Anatomically and functionally distinct microcircuits within subcortical and cortical visual areas register and process relevant pieces of information at a given retinotopic location. The products of these computations are then redefined in more sophisticated spatial reference frames (Gilmore and Johnson 1997) and utilised by more anterior brain areas to produce unified percepts that are classified as familiar or new. These percepts are the basis of visual learning, visual memory and visually guided action.

The non-human primate visual system has been extensively investigated and findings are often extrapolated to the human visual system. Macaque and human vision is comparable psychophysically with the exception of a small difference in long wave photopigment (Tootell et al 1996). Gross anatomy is also similar, as is laminar and cytoarchitectonic organization (Horton 1984, Wong-riley et al 1993). Differences do exist however, and relevant discrepancies will be highlighted. Although some reference to basic functional properties will be included, functional anatomy of higher order visual processing will be addressed in subsequent chapters.

1.1.1 The retina - early visual processing

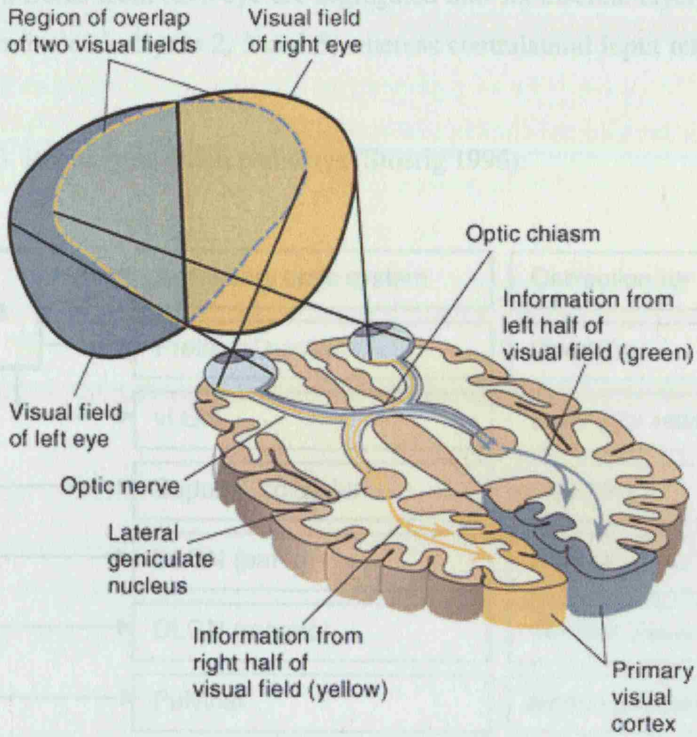
The initial segregation of different elements within the visual scene begins at the retina (Masland 2001), providing discrete channels of input that can be directed onwards to relevant subcortical and cortical processing centres. The retina is a laminar structure composed of many parallel, anatomically equipotent channels (figure 1.1). Light is transduced into an electrical signal by rod and cone type photoreceptors in the bacillary layer at the back of the retina. The two types of photoreceptor have different morphological and functional properties that contribute to initial segregation of visual input via retinal ganglion cells into parvo and magnocellular channels. Early segregation of visual input into basic elements affords rapid and effective processing in relevant cortical centres. As photoreceptors in a particular portion of the retina synapse with corresponding ganglion cells, the ganglion cells are said to have a receptive field that correlates with the area of the retina to which its photoreceptors are attached. Thus, the signals from ganglion cells contribute to a retinotopic map, as the collective pattern of firing from ganglion cells is a topographic illustration of the retinal areas that have been stimulated.

Figure 1:1. Structural anatomy of the retina (Tamarkin 2005)



It is important to outline the relationship between regions of the visual fields and the retinal image (figure 1.2). Firstly the lens of the eye inverts the image hence the superior half of the visual field is represented on the inferior half of the retina and vice versa. The surface of the retina is also divided into two halves with respect to the fovea, which represents the centre of the horizontal and vertical visual field. The temporal hemiretina is lateral to the fovea, the nasal hemiretina medial to it. Retinal ganglion cells exit the retina as the optic nerve, which passes backwards and medially through the orbit and optic foramen to the optic chiasma. Within the chiasma, the optic nerves partially decussate. Fibres from the nasal hemiretinae cross to the contralateral optic tract, whereas fibres from the temporal hemiretinae remain ipsilateral. Each optic tract is thus a combination of nerve fibres; the left optic tract is comprised of uncrossed fibres from the left temporal hemiretina, and crossed fibres from the right nasal hemiretina, representing the right field of vision. The right optic tract is comprised of uncrossed fibres from the right temporal hemiretina, and crossed fibres from the left nasal hemiretina, representing the left field of vision.

Figure 1:2. Nasal and temporal retinal projections to left and right visual fields (Carlson 2004).

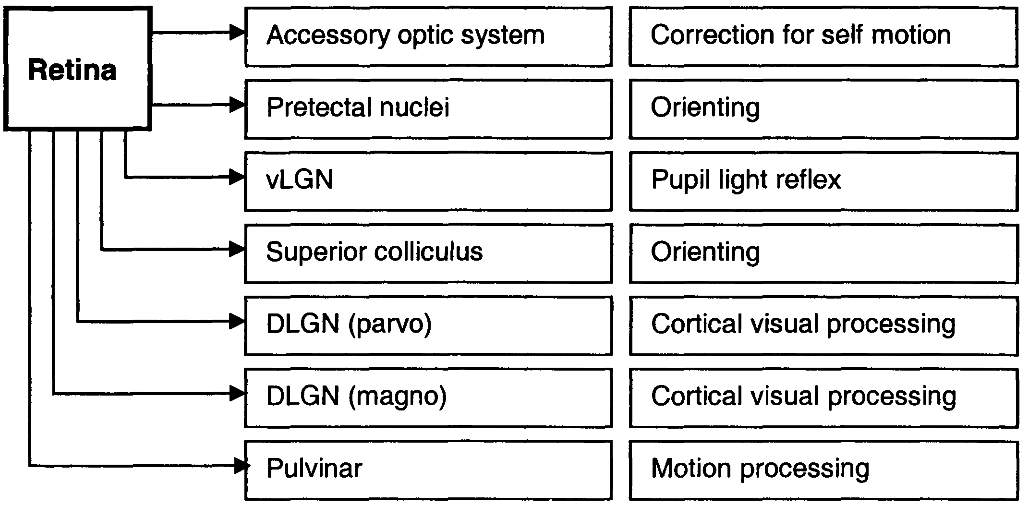


It is possible that anomalous ganglion cell projections (uncrossed nasal and crossed temporal projections) create a narrow zone of naso-temporal overlap that is believed to exist in the region of the retinal vertical meridian (Stone et al 1973, Bunt et al 1977). Fukuda confirmed the presence of crossed temporal and uncrossed nasal projections in the macaque using retrograde tracing and electrophysiological recordings (Fukuda et al 1989). The zone of overlap extended from just 0.6 deg in the central retina, increasing to 15 deg in the upper periphery and 5-9 deg in the lower periphery. Field mapping studies in human hemianopes also support the existence of naso-temporal overlap, (Fendrich et al 1996, Wessinger 1996) which spans approximately 2^0 either side of the vertical meridian, with a greater density in the upper hemiretinae. It is possible that such overlap could play a role in midline stereopsis (see chapter 3), although it remains to be confirmed.

1.1.2 Retinal projection pathways

The optic tracts have several projection targets that are illustrated in Fig 1.3. (Stoerig 1996). The three principal projection areas are the superior colliculus, the pretectal area and the dorsal lateral geniculate nucleus of the thalamus (dLGN). The main retino-cortical projection route is the retino-geniculo-striate pathway. The dLGN serves as the gateway for retinal signals en route to cortical structures, though its functional role as a passive relay station versus active modulation of retinal signals remains uncertain (Vidyasagar and Urbas 1982, Thompson et al 1994). The projection from the retina to the dLGN maintains a topographic organization such that the retinal impression of the visual field is mapped point to point onto the dLGN. Within the dLGN, fibres from each eye are segregated into six discrete layers. Ipsilateral input into the dLGN terminates in layers 2, 3 and 5, whereas contralateral input terminates in layers 1, 4 and 6.

Figure 1:3. Retinal projection pathways (Stoerig 1996).



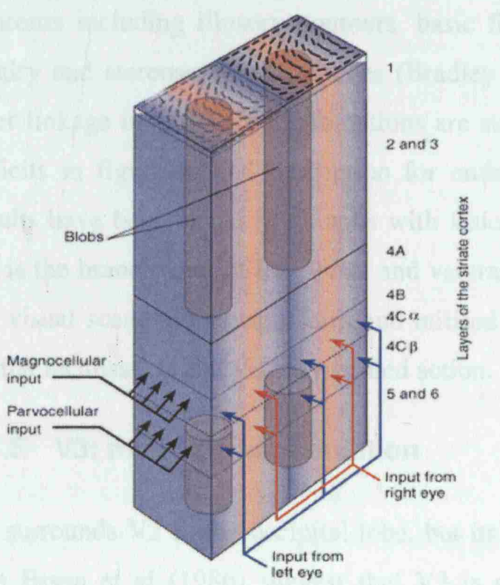
Furthermore, retinal ganglion cell input also remains separate in the dLGN. The beta ganglion cells from the retina convey chromatic, high spatial-low temporal frequency information and tend to arborise layers 3 - 6 as the parvocellular visual pathway. The alpha ganglion cells convey signals relating to luminance, low spatial frequency and high temporal frequency and project to layers 1 and 2 as the magnocellular visual pathway (Leventhal et al 1981). Thus, signals related to chromaticity and high spatial frequencies are loosely segregated from signals that relay contrast, low spatial frequencies and motion. There is however, some functional overlap between the magno and parvocellular pathways with respect to coding brightness, stereoscopic depth cues, texture, pattern, shape and flicker, suggesting the two pathways may in fact represent different extensions of the same functional system. The advantages of an extended basic system would include increased sensitivity to high spatial (parvo) and temporal (magno) frequencies whilst allocating a substantial proportion of neural substrate to intermediate frequencies (Schiller 1996).

The projections from the dLGN radiate along the lateral surface of the temporal and occipital horns of the lateral ventricle to primary visual cortex (V1 or Brodmann Area 17), the so-called gatekeeper of the cortical visual systems. The inferior aspect of the retina (upper visual field) is represented in projections to the inferior bank of the calcarine fissure. The fibres relaying input from the superior aspect of the retina (lower visual field) terminate in the superior bank.

1.1.3 V1: the cortical gatekeeper

V1 or striate cortex is a complex mosaic of specialised groups of cells, whose collective pattern of activity provides basic information pertaining to wavelength, orientation, contrast, motion and depth (Schiller 1996). The retinotopic map of the contralateral visual field in the dLGN is preserved within V1. As a result, V1 focal lesions cause blindness in the corresponding part of the visual field, and unilateral ablation of V1 results in a contralateral homonymous hemianopia. V1 is described as a hexalaminar structure (see figure 1.4). Axons from the dLGN generally terminate in layer 4, which is further divided into 4 layers: 4A, 4B, 4Cα, and 4Cβ. Magnocellular input projects mainly to layer 4Cα, while parvocellular input projects mainly to layer 4Cβ (Fitzpatrick et al 1994). The neurophysiological properties of cortical cells above and below layer 4 begin to diverge from their counterparts in the dLGN. Cells appear to respond optimally to stimuli that are more complex than those that excite cells in the retina and dLGN. Receptive fields are elongated rather than circular, reflecting preference for linear stimuli and orientation selectivity, and some cells have binocular receptive fields (Snodderly and Gur 1995). The distinction between Magno and parvocellular systems also declines (Merigan and Maunsell 1993), reflecting an increase in convergence and integration of information within the visual system, the necessary pre-requisite for building unified percepts that will eventually manifest as complex mental representations.

Figure 1:4. Hexalaminar module of V1 (Livingstone and Hubel 1984).



In summary, primary visual cortex appears to be the principal recipient of visual information from the six layers of the dLGN, which is distributed to cells coding for basic elements of the visual scene. The basic distinction between signals in the magno and parvo cellular streams appears to be retained as information proceeds beyond V1 and reaches the stripe system of V2, though some functional overlap is apparent. Direct feed forward projections from V1 have been traced to V2, V3, V4, V5 and the frontal eye fields in primate studies (Lund 1975, Maunsell and van Essen 1983, Ungerleider and Desimone 1986, Perkel et al 1986, Shipp and Zeki 1989, Fitzpatrick 1994). Direct feedback projections to V1 originate from V2 – V5, frontal eye fields, lateral intraparietal areas and inferotemporal cortex (Ungerleider and Desimone 1986, Perkel et al 1986, Shipp and Zeki 1989, Rockland 1994, Barone 2000, Suzuki 2000), and there are feedback projections from V1 to the dLGN, SC and pons (Gutierrez and Cusick 1997, Lund 1975). The extent to which information is processed in V1 remains controversial. V1 has been described as a passive recipient and distributor of information, yet also as a crucial mediator in visual awareness via top down connections with more anterior brain areas, and its inherent capacity to process static achromatic form (Tong 2003).

1.1.4 V2: grouping of elements

Human V2 surrounds V1 in the occipital lobe, is approximately homologous to macaque V2 (Tootell et al 1998), and contains a retinotopic map. The magno and parvocellular divisions from V1 are partially segregated in the stripe system of V2 (Tootell et al 1995). Parvocellular neurons from V1 project to thin stripe and interstripe areas in V2, which in turn project to V4 and thence to inferior temporal cortex to form the ventral visual pathway (Young 1992). The Magnocellular projections from V1 arborise in the thick stripe regions of V2. There is extensive crosstalk between stripe and interstripe regions however, thus eroding the segregation of magno and parvocellular pathways. The principal functions of V2 appear to relate to grouping of contours including illusory contours, basic figure-ground perception and resolving binocular rivalry and stereoscopic depth cues (Bradley 2001). Object contours are thus passed forward after linkage in V2. These assumptions are supported by macaque lesion studies that illustrate deficits in figure-ground perception for embedded figures (Merigan et al 1993). Analogous results have been found in humans with lesions in extrastriate areas (Rizzo and Robin 1990). V2 is the branchpoint of the dorsal and ventral processing streams, where different elements of the visual scene are carried forth and utilised for different tasks, namely object identification, spatial localisation and visually guided action.

1.1.5 V3: motion and orientation

V3 surrounds V2 in the occipital lobe, but its precise anatomical extent is still under scrutiny. Van Essen et al (1986) suggest that V3 is somewhat incomplete ventrally in primates and therefore its retinotopic map represents only the lower half of the visual field. He concludes that V3 is a vestigial piece of the visual system that is now functionally redundant, as its representation is highly variable across different primates. Kaas and Lyon (2001) argue that V3 exists as a complete representation of the visual field, but is split into separate dorsal and ventral halves. Macaque single cell recording studies illustrate motion and direction selectivity in the receptive fields of putative V3 cells, which suggests an association with the dorsal visual processing stream. Several human PET studies demonstrate motion selective activity in the regions immediately superior and posterior to V5, which may correspond with the locus of V3 in humans (Watson et al 1993, Dupont et al 1994, De Jong et al 1994, Shipp et al 1994).

1.1.6 V4: colour processing

Human V4 is believed to be situated in the posterior aspect of the fusiform gyrus in the ventral occipital lobe (Zeki et al 1991). Extrapolations from macaque studies suggest V4 receives parvocellular projections from V2 (Howard 2000), and thus codes for colour and form. V4 has also been implicated in shape, depth and motion processing (Schiller 1991, 1994). Although there is some discrepancy between human and macaque data with respect to localisation and function (Tootell 2001), human lesion studies show that this area is critical for the phenomenal experience of colour (Zeki and Bartels 1999, Heywood et al 1992), whereas the macaque V4 homologue is more closely related to form processing (Zeki 1977, Schein and Desimone 1990) and colour constancy (Kulikowski 1994). Another interesting observation with respect to V4 lesions in macaques is the deficits related to disembedding target objects from a complex array of competing stimuli (Schiller 1993, Merigan 1996) suggesting V4 may be involved in advanced figure-ground perception.

1.1.7 V5: motion processing

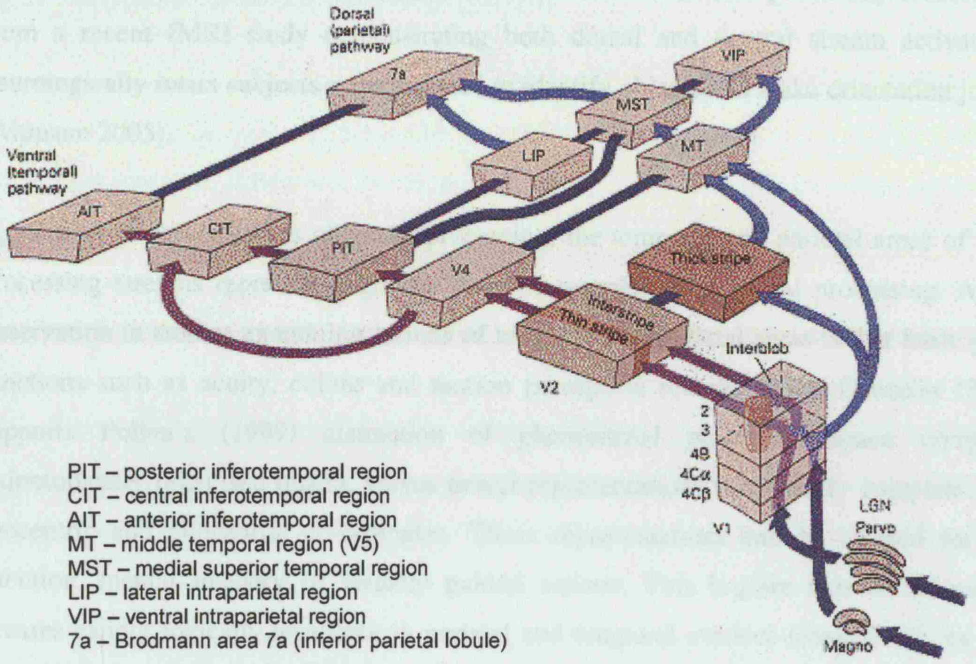
The human homologue of V5 is situated in the region of the middle temporal gyrus, on the convexity near the occipito-temporal junction (de Yoe 1994). fMRI studies of neurologically intact adults and behavioural studies in patients with cerebral lesions imply that this area is critical for the phenomenal experience of motion (Tootell 1995, Snowden 1992). Motion in V5 is detected via changes in luminance, colour and texture, which illustrate the fact that these stimulus properties are not processed exclusively in separate functional pathways.

Cortical areas V1-V5 have been described as structurally distinct modules, each with its own functional specialisation. Admittedly, this is a simplification to produce some kind of descriptive clarity on such a complex system. It is possible that most neurons are not dedicated to analysis of a single attribute from a single location, instead having multipurpose functions that integrate information over a considerable topographic area (Schiller 1996). Specificity may be achieved by discrepancies in spatio-temporal patterning of signals for different attributes of the scene. Whilst this cannot be refuted, there is enough evidence from lesion studies to provide at least some evidence for functional segregation within the visual system (see section 1.4). With regards to processing in areas V1-V5, products of computations within these regions may give rise to basic sensations such as brightness, colour or motion qualia, producing a phenomenal perceptual space comprising retinotopically localised stimuli (Pollen 1999). An ongoing quandary in visual neuroscience is how these basic, precisely localised elements of the visual scene are recombined after initial encoding to produce meaningful, coherent percepts that contribute to recognition and subsequent action. Crosstalk between magno and parvocellular systems has been alluded to. There is also a progressive decrease in retinotopic precision from V1 to more anterior and lateral brain areas, enabling image selectivity across distant receptive fields. This could be a crucial step in orchestrating the binding process of discrete patterns of activation in order to produce co-ordinated patterns of activity that will appeal to templates stored in higher processing centres.

1.1.8 The cortical processing streams – the dorsal and ventral visual pathways

There are several ways of conceptualising cortical visual processing. So far, cortical areas of the visual system have been described as discrete, functionally specialised modules that process particular elements of the visual scene. Another method of describing the functional geography of the visual system is that of two parallel processing streams that mediate space and object processing, thus linking discrete modules together according to their relative specialisations. Schneider (1969) originally proposed separate geniculo-striate and retino-collicular processing streams for object identification and spatial behaviour respectively. This model was redefined by Ungerleider and Mishkin in 1982, to reveal two cortical processing streams (figure 1.5). Results were derived from monkeys with focal cerebral lesions, and enabled localisation of critical regions within the two streams. The dorsal stream is predominantly magnocellular, though a small parvocellular component also exists. It runs from V1 layer 4Cα to V1 layer 4B towards the thick stripes of V2 and then onwards to medial temporal cortex and posterior parietal cortex. This stream was thought to be responsible for processing of spatial information. The ventral stream has a mixed magno and parvocellular input. It runs from V1 layer 4Cβ to blobs and interblobs of V1, onwards to thin stripe and interstripe regions of V2, which are thought to project to V4, then posterior inferior temporal cortex (TEO and IT in the macaque). This stream was thought to be responsible for visual recognition. The anatomical segregation of the two streams has been repeatedly confirmed in primate studies (Felleman and Van Essen 1991, Young 1992) and the model was reviewed by Ungerleider in 1994 to incorporate the observation that spatial processing could be parsed into spatial localisation and visuomotor control.

Figure 1:5. Dorsal and ventral processing streams (Carlson 2004).



Goodale and Milner (1992, see also Goodale and Westwood 2004) also suggested further modifications to the model. They re-defined it as a system in which each stream uses the same information but for different purposes. The function of the ventral stream was to encode features and contours within egocentric and allocentric reference frames to enable object identification. The dorsal stream was responsible for encoding spatial information within an egocentric frame of reference for directing visuomotor action, and using either frame of reference to compute spatial transformations of percepts and images.

fMRI studies of neurologically intact individuals and behavioural studies of patients with focal cerebral lesions provide converging evidence for the distinction between dorsal and ventral stream function. fMRI studies in neurologically intact human subjects demonstrate cortical activation in occipito-temporal regions for tasks requiring attention to colour and form (Bartels and Zeki 2004, Gauthier 2000, Valyear et al 2006), and posterior parietal activation during spatial tasks (Milner and Goodale 1996, Kosslyn 1998, Grefkes and Fink 2005, Valyear et al 2006). Clinical observations have shown that spatial computations and visually guided action is disrupted in patients with posterior parietal lesions (Ratcliff 1972, Perenin 1988) yet object identification may remain intact (Jakobson 1991). Patients with inferior temporal lobe lesions have difficulty with visual form discrimination and recognition (Campion 1987, Milner 1991), yet internal manipulospatial functions and visuomotor behaviour may seem unimpaired (James et al 2003). The two systems are however, not entirely distinct; It is possible that both dorsal and ventral streams receive signals pertaining to form and spatial co-ordinates, and through a dense network of interconnections, work closely together to achieve the specific task at hand rather than remaining entirely segregated (Jeannerod 1997). This possibility receives support from a recent fMRI study demonstrating both dorsal and ventral stream activation when neurologically intact subjects were required to identify objects and make orientation judgements (Altmann 2005).

In contrast to earlier stages of visual processing, the temporal and parietal areas of the visual processing streams represent a greater level of complexity in visual processing. A common observation in studies examining lesions of temporal and parietal areas is that basic perceptual functions such as acuity, colour and motion perception remain intact (Damasio 1990). This supports Pollen's (1999) distinction of phenomenal perceptual space comprised of retinotopically organised qualia, versus neural representations that specify complete objects in egocentric and allocentric co-ordinates. These representations can be utilised for selective attention, mental imagery or visually guided actions. This implies that dorsal and ventral streams cannot logically terminate in parietal and temporal cortices respectively, as attention, response selection and motor functions are consistently associated with the frontal lobes (Nobre 2001, Astafiev 2003). Indeed, the dorsal and ventral streams do not terminate in parietal and temporal cortices respectively. They continue onwards, the dorsal stream projecting to the premotor, dorsolateral and dorsomedial prefrontal cortex, and the ventral stream projecting to ventrolateral and orbitofrontal cortex (Barbas 1988, Webster 1994). Neuroimaging studies indicate that these frontal regions retain their specialisation for spatial and object vision respectively (Courtney et al 1996, Pihlajamaki 2005)

In summary, the visual system has been outlined as a hierarchical, parallel processing system. Parvo and magnocellular pathways convey different types of information from the retina to subcortical structures, notably the dLGN, and cortex. Functional subdivisions have been observed in V1 and V2, after which the retinal parallel pathways are recombined into two major cortical visual processing systems. The occipital- parietal or dorsal system mediates rapid, on line visually guided action and complex judgements of spatial attention, localisation and manipulation. The occipito-inferior temporal or ventral system mediates object recognition. Feed forward, feedback and horizontal connections between streams enable rapid construction of complex representations that contribute to recognition of different elements of the visual scene and registration of their relative positions in space for subsequent goal directed actions.

1.2 Development of the visual system

1.2.1 Overview of structural development

The mature human visual system is a product of carefully orchestrated developmental processes. The basic layout of the retina resembles that of an adult at 11 months (Mc Culloch 1998). Ganglion cell axons exit the retina and segregate at the optic chiasma. As optic fibres emerge from the chiasma, they segregate according their parvo or magno ganglion cell origins. This parvo-magno segregation is preserved at the dLGN, where parvocellular layers become innervated before magnocellular layers. The segregation of laminae in the dLGN is thought to be dependent on bursts of endogenous ganglion cell activity arising in the prenatal retina, as synapses firing in synchrony reinforce each other and suppress activity that is out of phase. The discordant patterns of activity allow segregation of the two types of ganglion cells into distinct layers in the dLGN. Projections from the dLGN reach layer 4 of the 6 layered neocortex of V1, which is the principal recipient layer.

Although incomplete, the elementary circuits created as a result of endogenous neural activity during prenatal life enable some responsiveness to visual stimuli at the time of birth. Most of the basic structural and functional elements of the visual system become functional during the first year of life (Howard 2002). Spontaneous discharges that influence initial connectivity within the visual system are replaced by stimulus dependent neural activity that enables fine tuning of the whole system. Connections between cells within the main cortical layers demonstrate evidence of early excess followed by elimination, which is a reflection of tuning of cortico-cortical connections via detection of synchronous activity. As synaptic density increases over the first 8 months of life, the visual system demonstrates increasingly sophisticated levels of function as evidenced by enhanced spatial and temporal resolution (Beazley 1995). Elimination of aberrant connectivity ensues until the end of the first year, at which point synaptic density resembles adult levels. Synaptic connectivity then undergoes extensive remodelling throughout the first decade of life before approximating adult synaptic profiles (Huttenlocher and de Courten 1990).

1.2.2 Models of functional development of the visual system

Bronson (1974) proposed a two systems theory for the developing visual brain that is closely akin to Schneider's model (see section 1.1.8). The primary visual system is cortically mediated, represented maximally in the fovea and has excellent acuity. It is devoted to fine grain pattern analysis. The secondary visual system is phylogenetically older and subcortically mediated. It has poor acuity and responds optimally to rapid onset/offset or moving targets in the periphery.

The secondary system is relatively mature at birth and its functional properties characterise the limits of neonate visual behaviour. The emergence of sensitivity to fine visual detail, attention to forms and objects, and memory for patterns between 2-12 months of age was believed to reflect the emergence of primary visual system function. Although Bronson's model is a somewhat simplified and incomplete account of early visual development, it still serves as a useful framework in understanding the relationship between brain development and visual behaviour during infancy.

In parallel to the modifications of Schneider's model of visual processing by Mishkin and Ungerleider, Atkinson (1992, 2003) redefined Bronson's model to incorporate divisions between magno/parvocellular streams and dorsal/ventral cortical streams in addition to subcortical/cortical visual processing. The original disparity between emergence of subcortical and cortical vision is upheld, in addition to the proposal that different elements of the retino-geniculo-cortical system may have different developmental courses, and that different facets of major processing streams may also emerge at different stages in development. The trajectory of cortical and subcortically based visual processing in Bronson's and Atkinson's models receives support from several lines of evidence. Neonatal vision is characterized by poor acuity, limited visual attention, sporadic saccades and inaccurate fixation (Daw 1995), which suggests that cortically based oculomotor and attentional mechanisms are immature and/or constrained by degraded input from the immature retina. There is also a distinct preference for salient, peripherally situated stimuli that are of rapid onset, which accords with subcortical orienting mechanisms (Atkinson 1992). A gradual improvement in acuity, improved oculomotor competence and increased interest in faces is observed between 2-6 weeks, with improvements in ocular alignment and central fixation between 6 weeks and 3 months, which implies that improved quality of input may appeal to more sophisticated neural substrates. Binocular fusion, optokinetic nystagmus and sensitivity to isoluminant colours also become apparent between 2-3 months. Improved efficacy of saccades and pursuit, stereoscopic vision and evidence of reaching for toys become apparent between 3-5 months (Hainline 1998), which reflects integration between visual and oculomotor systems and subsequent goal directed action.

Atkinson suggests that the parvocellular system comes into operation earlier than the magnocellular system. This has been illustrated by orientation discrimination experiments in neonates. Although neonates are able to detect changes in orientation, there is a temporal constraint, with only slow changes being detected (Hood 1992). At around three months of age, a greater repertoire of visual skills become evident, such as detection of rapid changes in orientation, and detection of relative direction of motion. This is conceptualised as the gradual appearance of magnocellular stream activity, and the shift towards greater involvement of cortically based visual processing. Although the discrepancy between cortical and subcortical vision in the Bronson and Atkinson models appears to blend well with experimental findings, the suggestion of earlier emergence of the parvocellular component of the retino-geniculo-striate pathway in Atkinson's model does not accord with observations that early vision is rod based (Teller 1982), which implies that magnocellular activity may in fact precede parvocellular activity. Evidence for rod based function is based on the fact that scotopic spectral sensitivity in 1 month old infants closely resembles that of adults and that sensitivity to chromatic stimuli follows a relatively protracted course of development (Allen 1993). It is possible that early predominance of simple magnocellular processing is superseded by parvocellular activity, with more complex functions related to the magnocellular stream emerging a few months later. Further information is needed to clarify the relationships between behavioural and psychophysical studies, and the possibility of magno and parvocellular streams predominating at different points in early development.

In turn, Atkinson also proposes that dorsal and ventral streams have different maturation gradients. From an initial subcortical stage of orienting to salient peripheral stimuli, cortical visual processing circuits become established and interconnected within the ventral stream, with subsequent contributions from the dorsal stream regarding control of head and eye movements. Object representations within the ventral stream are integrated with motion and disparity information to enable emergence of dorsal stream circuitry responsible for visually guided actions such as reaching, grasping and locomotion. Perceptual matching and discrimination of shapes in the ventral stream appears to emerge earlier than constructing an appropriate series of motor commands based on the same perceptual information in the dorsal stream. Early preference for faces may also be interpreted as evidence for relative precocity of ventral stream function, though alternative suggestions of a subcortical basis for such preferences must be acknowledged (Morton and Johnson 1991, Simion 1998). Atkinson suggests that the gulf between the two streams appears to become much narrower between 5 and 7 years of age, as improvements in visually guided reaching and grasping become more precise. The nature of the delay of functional maturation in the dorsal stream is related to the complexity of spatial reference frames used for visually guided action, and their dependence on acuity, contrast sensitivity (Banks 1987), and mature eye movement programming and stability of head position (Bloch 1992). Within the first few months of life, each of these spatial reference frames become more accurate due to gradual calibration between maturing visual and motor systems. There is no comparison to the development of viewpoint independent reference frames within the ventral stream, which are not completely developed at 7 years of age (Temple 1997). Thus it seems possible that although a gulf between relative integrity of dorsal and ventral processing streams may be apparent in early childhood, a more detailed description of functional maturity is needed before definitive conclusions can be reached in terms of the protracted course of development of the dorsal stream.

In summary, the development of the visual system involves gradual evolution from a predominantly subcortically based system to cortical processing. Marked improvements occur at approximately 2-3 months of age when a variety of perceptual functions emerge such as binocular fusion, chromatic sensitivity and improved oculomotor functions such as tracking, accommodation and vergence. These perceptual functions continue to mature and reach adult levels between 5-9 years of age, with possible discrepancy between rates of maturation of dorsal and ventral streams. Visual cognitive functions such as face processing, mental rotation and construction follow a more protracted course of development, which extends into teenage years (see chapters 5-7). It follows that brain injury sustained during childhood may affect a multitude of developing visual functions, as different levels of maturity in different components of the visual system may result in failure to develop functions not previously established, premature arrest of functions that are still developing, and loss of functions already established. The consequences of such injuries are discussed in section 1.4.

1.3 Laterality of visual cognitive function

1.3.1 Structural hemispheric asymmetry

There is a robust association between structural and functional divisions of the visual system within a cerebral hemisphere. Morphological differences between photoreceptors and the nature of their associated circuitry predispose each type of receptor to conveying different kinds of information. The same observations can be made for different types of retinal ganglion cells, parvo and magnocellular streams, blobs and interblob regions of V1 and the stripe system of V2. It is therefore not unreasonable to suggest that structural differences observed between the left and right hemispheres may be indicative of possible functional differences. Indeed, Trevarthen (1996) concluded that cerebral asymmetry of perceptuo-cognitive functioning is most likely to stem from embryogenic asymmetries of anatomy and pharmacology. Several lines of evidence converge to suggest that structural and functional differences are indeed apparent, though evidence is sparse and direct relevance to visual perception and cognition remains to be illustrated. Several investigators have found chemical asymmetries between the hemispheres. Tucker and Williamson (1984) claimed that left hemisphere has an abundance of dopaminergic terminals respectively, which has been replicated in post-mortem studies of the basal ganglia (Glick 1982). Studies of children with disrupted dopaminergic metabolism (Craft et al 1992, Heffelfinger et al 1997) showed attentional deployment to the right visual field was disparately affected, suggesting the left hemisphere visual attention system is disproportionately affected by disruptions of dopaminergic metabolism. Tucker and Williamson suggested that the left hemisphere became organised around a dopaminergic activation system that resulted in affinity for complex motor programming and thus right handedness and speech. The same authors also found a relative abundance of adrenergic terminals in the right hemisphere, which has been echoed at least in studies of thalamic nuclei (Oke 1978 but see Nyberg et al 1982). The right hemisphere is thought to become organised around an adrenergic system that predisposes towards alertness and orientation to novel stimuli, in addition to integration of bilateral perceptual information. Excessive right hemisphere noradrenergic activity has been implicated in Attention Deficit Hyperactivity Disorder (ADHD) (Malone et al 1994) and novel ADHD treatments include noradrenergic blockers (Purper-Ouakil et al 2005).

Gross anatomical asymmetry has been documented for over a century (Erberstaller 1884, Cunningham 1892). Counterclockwise torque results in the right frontal lobe being slightly larger than the left frontal lobe, and the right occipital lobe is slightly smaller than its counterpart on the left (LeMay and Clebras 1972, Bradshaw and Nettleton 1983). The greater length and reduced curvature of the sylvian fissure in the left hemisphere has been observed in adults and children (Geschwind and Galaburda 1985, Seidenwurm et al 1985, Hellige et al 1998), in fact asymmetries of the planum temporale have been observed as early as 30 weeks gestation (Chi 1976, Preis et al 1999). The pars opercularis in the frontal lobe is larger in the left hemisphere, whereas area PG in the parietal lobe is larger in the right hemisphere (Eidelburg and Galaburda 1984). A recent MRI study (Watkins 2001) demonstrated that in addition to classically described sylvian fissure asymmetries, the cingulate sulcus, anterior insular cortex and caudate nucleus were larger in the right hemisphere. Further neuroimaging studies are needed to determine whether structural asymmetries are directly correlated with functional asymmetries of visual perception and cognition.

1.3.2 Functional hemispheric asymmetry and visual cognition

In addition to chemical and structural differences between the hemispheres, functional asymmetry is indeed evident. Results from neurologically intact individuals using tachistoscopic methods and neuroimaging, and observations of patients with focal unilateral lesions converge to support the idea of functional differences between the hemispheres. .Miossec (1993) and Banich (2000) propose that only later stages of processing are asymmetric, with either hemisphere being equally competent in the early stages of perceptual processing. Their claims stem from studies of neurologically intact individuals that demonstrate no visual field preferences for simple perceptual judgements. Symmetry in early perceptual functions makes adaptive sense in a complex environment, as stimulus location is often unpredictable. Whilst complex processing of perceptual input may benefit from complementary specialisations of the cerebral hemispheres, it is clearly advantageous for both hemispheres to be equally receptive to sensory input so that attention may be drawn to the left or right visual fields as required. Whilst the majority of studies documenting functional asymmetry are in fact based on processing of complex stimuli such as faces (Rossion 2000, 2003), others utilise relatively simple discrimination tasks using grating stimuli (Han 2002).

The right hemisphere is often regarded as being dominant for non-verbal functions. In a recent meta-analysis of cerebral laterality of function, Vogel et al (2003) conclude that the right hemisphere is dominant for spatial processing, but acknowledge that considerable variance exists across studies. The right hemisphere is more sensitive to low spatial frequencies (Han 2002) and is preferentially involved in spatial awareness and attentional vigilance (Posner 1992, Manly et al 2005 see chapter 4), face processing via sensitivity to configural properties of faces and recognition of familiar faces (Le Grand 2003, Rossion 2003 see chapter 5), computing spatial location using allocentric co-ordinates (Maguire 1998, Fink et al 2003), locating stimuli in co-ordinate space (Kosslyn 1992, Jager and Postma 2003 see chapter 6), attending to global aspects of complex figures (Martinez 1997), mental rotation (Corballis 1997, Harris et al 2003 see chapter 6) and recognizing stimuli that have been perceptually degraded (Sergent 1986). Drawings made by patients with right hemisphere injury (Warrington 1966, Stiles 1997), or drawings made by the right hand in callosotomy patients (Gazzaniga 1970, 1985) often display lack of spatial coherence (see chapter 7). Performance is also poor on block design tests in these two patient groups (Bogen and Gazzaniga 1965, Gazzaniga and Le Doux 1978, Stiles and Nass 1991, Schatz et al 2000).

Relatively little attention has been devoted to investigating visuospatial functions of the left hemisphere. The left hemisphere is believed to be sensitive to high spatial frequencies (Han 2002), and specialised for featural aspects of face processing (Rossion 2000 see chapter 5), locating stimuli in categorical space (Kosslyn 1992, Jager and Postma 2003 see chapter 6), attending to local aspects of complex figures (Martinez 1997), and computing left-right relationships in relation to ones own body (Benton 1968, Zacks 1999 see chapter 6). Drawings of patients with left hemisphere injury (Warrington 1966, Stiles 1997), or drawings made by the left hand in callosotomy patients (Gazzaniga 1970, 1985) are spatially coherent but often lack detail (see chapter 7). Object identification is also thought to be superior in the left hemisphere as evidenced by right visual field advantages in object identification tasks (Vitkovitch 1992), and increased tendency to demonstrate object agnosia after left hemisphere lesions (Farah 1990).

When thinking of cerebral asymmetry, it is also important to acknowledge the fact that the two hemispheres function as a part of a unitary system. The left and right hemispheres appear to co-ordinate their activities such that different elements of complex tasks will be mediated by the hemisphere that is most adept at that particular facet of processing (Belger and Banich 1998). The corpus callosum is believed to play a critical role, both in transfer of information across the hemispheres, and gating of information that would result in mutual interference (Kinsbourne 1982). It is possible that simple tasks may be mediated principally by one hemisphere, with communication of the products of processing to the other hemisphere upon conclusion (Hardyck 1985), but when task complexity increases, callosal gating mechanisms may allow transfer of information between the hemispheres to ensure optimal information processing (Green 1984).

1.3.3 The nature of hemispheric asymmetry

Classic dichotomies used to conceptualise the nature of cerebral asymmetry such as verbal-non verbal, analytic-holistic, and focal-diffuse have been replaced with the notion of complementary specialisation, whereby each hemisphere may possess basic functional capacities in most cognitive domains, but the limits of sophistication and level of predisposition to particular modes of processing may differ. In this manner, the functional profiles of the left and right hemispheres may differ on a quantitative as opposed to qualitative basis, and when faced with a complex stimulus, it is most likely that both hemispheres play a role using complementary styles of information processing. Another important evolution in functional laterality research is the advent of more detailed investigation of the different sub-components of a particular task. It is possible that differences in hemispheric function may be apparent for some components and not others, therefore results on the task proper may mask subtle differences that manifest in certain elements of the task. Although hemispheric differences may now be investigated under a more realistic framework, the nature of these functional differences remains to be elucidated.

Semmes (1968) suggests that relatively focal representations of function in the left hemisphere would favour integration of similar adjacent units, leading to specialisation for behaviours that demand rapid sequencing of similar output nodes, whereas the diffuse representation of functions in the right hemisphere enable integration of units that are widely distributed, leading to specialisation for behaviours that demand multimodal co-ordination and integration of information across distant brain regions. Whilst this theory was originally proposed as a contribution to the dichotomania of the scientific era, its principal tenets are still useful in considering possible differences in processing styles of the two hemispheres. Goldberg and Costa (1981) also suggest that the right hemisphere has more interregional connections whereas the left hemisphere has more intra regional connections. It follows that if neural development is disrupted and connectivity is lost or fails to develop, the right hemisphere is more likely to be significantly compromised due to the nature of its connective architecture. Indeed, there is some evidence to suggest that at least in early life, damage to the right hemisphere has particularly severe consequences (Neville 1999).

Another possibility is that differential sensitivity to certain types of input would influence subsequent processing styles in the left and right hemispheres. Various studies have revealed differences in spatial frequency preferences of the two hemispheres (Sergent 1982, Michimata and Hellige 1987, Christman 1990). The use of complex stimuli in these studies render the effects somewhat indirect due to the vast range of spatial frequencies available in the stimulus, the range of frequencies most relevant for the task at hand, and whether the relevant frequencies are higher or lower than other frequencies contained in the stimulus. Nevertheless, support from studies using gratings (Kitterle 1990, 1991, Christman 1991, Proverbio 1997) provide moderate support for differential sensitivity of the left and right hemispheres to higher and lower spatial frequencies respectively.

Several authors provide explanations for the existence of lateralisation of function in terms of adaptive benefits. Division of labour (Belger and Banich 1998) and affordance of highly specialised systems (Hellige 1993) are commonly cited examples, and the possibility of complex motor sequencing for the dominant hand providing a blueprint for the development of language in the left hemisphere. The concept of division of labour has received support from studies using clinical populations (Lamb 1990), and divided visual field studies in neurologically intact individuals (Green 1984, Banich and Belger 1990), but Floel (2001) reminds us that language and visuospatial function may be lateralised to the same hemisphere in neurologically intact individuals as evidenced by rCBF studies of linguistic and spatial tasks. There are also sporadic cases of "reversed laterality" whereby left hemisphere lesions result in visuospatial as opposed to verbal impairments (Junque 1986). The fact that language and motor control are not always situated in the same hemisphere as evidenced by the majority of left handers having left hemisphere language also creates problems for hypothetical relationships between left hemisphere language and motor function. It is therefore important to consider individual differences with respect to the direction and magnitude of hemispheric asymmetry. Although factors such as gender and handedness (McManus 2002) have been implicated in hemispheric asymmetries, evidence is mixed, with little consistent indication that laterality profiles are influenced by these factors.

1.3.4 Development of asymmetry

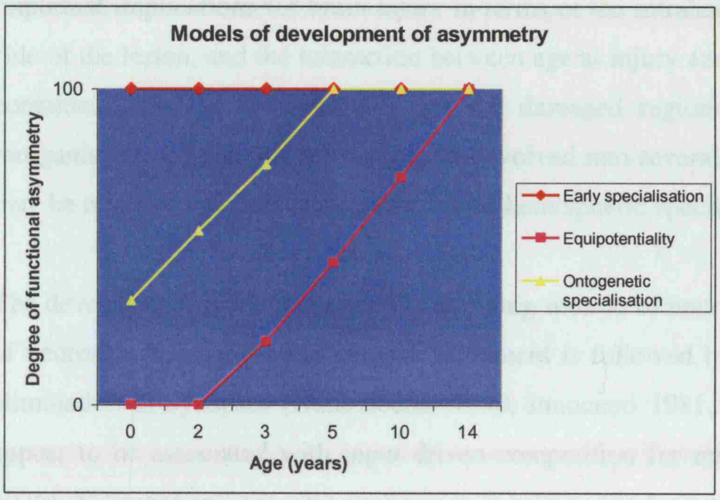
Debate exists as to whether hemispheric laterality exists in children, though available evidence indicates that structural asymmetries are present in prenatal life. Cortical landmarks of the sylvian fissure and folding of adjacent gyri appear later in the left hemisphere during foetal development (Fontes 1944, Chi 1977). Cortical landmarks of the superior temporal region also appear later in the left hemisphere (Chi 1977). Amaducci (1981) found adult levels of choline acetyltransferase in the right temporal lobe of human foetal brains at 29-30 weeks gestation, and was higher than levels in the left temporal lobe even in older foetuses. Scheibel (1985) found that the extent of higher order dendritic branching was greater in the left hemisphere, with lower order branching being longer in the right hemisphere, reflecting earlier development of the right hemisphere in early life. Several authors suggest that the relatively precocious development of the right hemisphere persists until the end of the second year of life (Semrud-Clikeman 1990), which accords with results from an rCBF study (Chiron 1997) that found greater flow in the right hemisphere, especially in parietal lobe, with subsequent shift to the left hemisphere at 3 years of age. Semrud-Clikeman (1990) suggests that earlier development of the right hemisphere results in specialisation for input that is encountered in early life, such as novel gestalts of low spatial frequency. Evidence is mixed, as others argue that postnatal development of the left hemisphere proceeds more quickly (Corballis 1978, 1991).

Functional evidence is mixed but some support for right hemisphere precocity is apparent in neurologically intact children. Fogel (1990) found that use of a left handed grip in 3 month old infants was associated with leftward attentional bias, whereas no attentional bias was observed when using a right handed grip, which suggests that the right hemisphere may be dominant for attentional control early in life. Indeed, visuospatial attention deficits in children have been attributed to right hemisphere lesions (Ferro 1990 see chapter 4), and childhood ADHD has been linked to right hemisphere dysfunction (Nigg et al 1997). Right hemisphere specialisation for faces is also thought to manifest during infancy (De Schonen and Mathivet 1990, Deruelle and de Schonen 1991) as 4-9 month old infants demonstrated a right hemisphere advantage in learning to discriminate between face stimuli. Processing of gender and emotion can be relatively poor after right hemisphere injury in childhood (Chiang et al 2000) and use of configural information in faces appears to be critically dependent on input to the right hemisphere during early development (Le Grand 2003 see chapter 5). Lateralised profiles similar to adults have also been found for global and local processing of visual stimuli (Schatz et al 2004, Moses et al 2002), categorical and metric processing (Koenig 1990 see chapter 6) and construction ability (Stiles 1997, Akshoomoff 2002, Schatz et al 2000 see chapter 7).

There are several models of the functional development of cerebral asymmetry (see figure 1.6). The equipotentiality hypothesis (Lennenberg 1967) claims that the two hemispheres are functionally equipotent until 2 years of age, after which hemispheric specialisation gradually develops and reaches adult levels in puberty. The early specialisation hypothesis (Witelson

1977) claims that hemispheric asymmetry is present at birth and remains stable across the lifespan. The intermediate view of ontogenic or interactive specialisation (Vargha-Khadem 1992, Johnson 2000) claims that although the two hemispheres are innately predisposed towards functional asymmetry, these tendencies become manifest over a period of time, such that a large amount of functional overlap is present in early life. The hemispheres are believed to demonstrate functional asymmetry at approximately 5 years of age (Vargha-Khadem and Mishkin 1997).

Figure 1:6. Models of development of cerebral asymmetry. X axis represents age, Y axis represents degree of hemispheric specialisation.



In summary, there are several lines of evidence to suggest that structural and functional asymmetry exists between the left and right cerebral hemispheres, some of which are present during infancy and childhood. Traditional conceptions of absolute hemispheric specialisation have been replaced with models of relative specialisation to allow for basic functional overlap between the hemispheres, with complementary processing styles becoming evident in more complex aspects of cognition. The nature of hemispheric functional asymmetry remains to be elucidated, but theories associated with differences in intrinsic connectivity and spatial frequency preferences remain attractive suggestions. Whilst evolutionary theories regarding adaptive benefits of hemispheric specialisation make intuitive sense, further study is needed to provide empirical support. Development of functional asymmetry may proceed along several different trajectories, ranging from innate specialisation to gradual development of functional asymmetry from equipotent cortex. These models have implications for the critical window of time in which neural plasticity may attempt to negate the effects of cerebral injury.

1.4 Plasticity and reorganisation of function

It is apparent that the visual system contains a vast and intricate arrangement of parallel processing systems that may be subdivided according to structural anatomy and functional specialisation. These components are ultimately subdivided into two major cortical processing streams that course dorsally and ventrally towards the frontal lobes to subserve spatial and object vision respectively. It is also evident that the visual system undergoes a protracted course of development, with basic perceptual functions such as stereopsis and acuity reaching maturity between 5-8 years of age (see chapter 3), and cognitive functions such as face processing and visuo-constructive skills maturing between 12-14 years of age (see chapters 5 and 7). In the mature visual system, hemispheric laterality of function is evident both structurally and functionally, and a limited amount of evidence suggests that the left and right hemispheres are also structurally and functionally different in the developing brain. These observations have important implications for brain injury in terms of the intrahemispheric locus of the lesion, the side of the lesion, and the interaction between age at injury and the level of maturity of systems contained within or coursing through the damaged region. The concept of plasticity and reorganisation of function after injury has evolved into several different lines of thought, which may be related to models of development of hemispheric specialisation outlined in section 1.3.

The developing brain is a continually evolving mosaic of neural circuits. Initial overproduction of neurones and synapses in early development is followed by cell death, axon retraction and elimination of synapses (Huttenlocher 1990, Innocenti 1981, 1986). These subtractive events appear to be associated with input driven competition for resources (Changeux and Danchin 1976). Neuronal and synaptic exuberance is believed to form the basis of the developing brains plasticity. Plasticity refers to a collection of processes that are dynamic, flexible and systematic, resulting in alteration of neural substrates to subserve learning in the neurologically intact brain, or reorganisation of function after injury.

1.4.1 Theories of hemispheric specialisation and response to injury 1: Equipotentiality

Debate exists as to whether functions usually subserved by the damaged region may be reorganised by utilising equipotent substrates, or whether fixed modular architecture results in region specific deficits that may be at best, sub optimally assumed by adjacent regions or homologous areas of the opposite hemisphere. Early observations of hemisphere specific deficits in adults in the 19^{th} century (Broca 1861, Dax 1865, Quaglino 1867) were challenged by authors arguing that no functions were localised strictly in any part of the cortex (Head 1926) and that cognitive deficits were a product of the amount as opposed to the region of damaged cortex, otherwise known as the mass action principle (Lashley 1929, 1963).

Hebb (1942) suggested that at least some degree of equipotentiality was evident in the developing cortex, as the effects of damage during infancy appeared to be diffuse and less selective than those observed in adults. An early injury that destroys substantial amounts of neural substrate creates a sub optimal system that may adversely affect development, yet an abundance of evidence exists for relative preservation of function when damage is sustained early in life. Broca (1865) had also conceded that although focal lesions to the left inferior frontal gyrus in the adult may produce persistent aphasia, similar lesions sustained during childhood might not prevent acquisition of language. Brown-Sequard (1877) also noted that children with brain injuries in regions classically associated with speech did not seem to demonstrate the same severe and persistent impairments observed in adults with similar lesions. These arguments were reiterated in subsequent years when considering brain injury during childhood (Alajouanine and Lhermitte 1965, Hammill 1966, Krashen 1973) with Lennenberg's (1967) theory of equipotentiality being the most influential argument for early similarity of the left and right hemispheres. His theory states that the two hemispheres are equipotent until 2 years of age, and gradually become specialised as development proceeds. It is also assumed that specialisation is accompanied by decreasing plasticity, such that by the time of puberty, side specific deficits appear after cerebral injury. Evidence for diffuse as opposed to sharply lateralised linguistic functions in the developing brain comes from studies of the normally developing infant, as diffuse, bilateral patterns of activity are observed during lexical processing in 13 month old infants, with progressive narrowing and lateralisation of active loci by 20 months (Mills et al 1997). Linguistic disturbances after right hemisphere injuries are also more prevalent in children than adults (Stiles 2000) and face processing deficits may be observed after diffuse, poorly localised lesions (Jones and Tranel 2001 see chapter 5).

Numerous studies documenting outcome after cerebral injury conclude that compensation or reorganisation of linguistic function may take place in the developing brain regardless of the side of the lesion (McFie 1961, Vargha-Khadem 1992, Goodman and Yude 1996). An important question relates to the costs of reorganisation of function in adjacent intrahemispheric regions or within the opposite hemisphere. Support for reorganisation of language in the right hemisphere is evident from reports of the crowding phenomenon (Teuber 1975), whereby functions classically ascribed to the right hemisphere are lost or diminished as a result of accommodating reorganisation of linguistic skills. Vargha-Khadem and Mishkin (1997) suggest that patients with congenital cerebral lesions cannot be differentiated according to side of lesions on tests of language, memory, visual perception, or frontal lobe functions. Whilst verbal IQ was not significantly impaired, performance IQ was impaired relative to neurologically intact controls whether lesions were left or right sided. Relative sparing of verbal functions were thought to be achieved at the cost of visuospatial function.

Whilst providing a loose theoretical framework for consideration of plasticity and reorganisation in the developing brain, Lennenberg's original estimate of hemispheric specialisation becoming evident in puberty was subsequently regarded as optimistic, with side specific deficits being reported after injury in children aged 5 years (Krashen 1973, Vargha-Khadem 2001), 2 years (Aram 1988) and before one year of age (Woods and Carey 1979, Witelson 1987, Vicari 1998). Lennenberg's data was also susceptible to diffuse generalisation regarding the degree of functional recovery of language. Although he suggested that complete recovery of language was evident when injury to the left hemisphere occurred before two years of age, more detailed studies reveal persistent deficits in syntactic functions after left hemisphere injury, regardless of time of insult (Vargha-Khadem et al 1985, Woods 1979, 1980, Stark 1995, Stark and McGregor 1997). Another difficulty in applying Lennenberg's theory to hemispheric reorganisation of function was its reliance on data from linguistic functions, providing no insight into possible outcome of visuospatial cognition after similar injuries. Thus, whilst the hemispheres may have some degree of functional overlap that permits reorganisation of basic linguistic skills in the right hemisphere, it remained unclear as to whether similar reorganisation occurred for visual cognitive skills after damage to the right hemisphere. Indeed, evidence for subtle yet persistent visuospatial impairments after cerebral injury have been demonstrated (Akshoomoff 2002, Stiles 1998, 2001). Banich (1990), Levine (1993) and Stiles (1997) also suggests that apparent lack of deficits in young children may reflect compensatory strategies that become less effective as more challenging tasks are presented and so apparent emergence of impairment later in life may simply be a result of unmasking of deficits already present.

1.4.2 Theories of hemispheric specialisation and response to injury 2: Early specialisation.

The alternative theory of early hemispheric specialisation has received attention from investigators documenting early differences between left and right hemispheres in neurologically intact infants, and side specific deficits after brain injury in childhood. As discussed in section 1.3, there are structural, developmental and functional differences between the left and right hemispheres evident during infancy and childhood. Evidence suggests that differential responses to lateralised stimulus inputs are evident during infancy (Molfese and Molfese 1980, Glanville 1977, Entus 1977, de Schonen and Mathivet 1990), though evidence is mixed (Novak 1989, Molfese 1991). Visual evoked potentials to flashes of light are stronger in the right hemisphere in 2 week old infants, an effect that persists throughout childhood and adulthood (Hahn 1987). De Schonen and Mathivet (1990) found a left visual field advantage when infants aged 18-42 weeks were required to learn discrimination between familiar and non familiar faces. They conclude that hemispheric asymmetry for face processing is established by

4 months of age. This contrasts with studies mentioned previously that demonstrate relatively diffuse representation of language at this age. Hemispheric asymmetries relating to face processing appear to be less apparent in children aged around 8 years of age (Levine 1985), but this is attributed to changes in cognitive strategy, such as feature based processing, with classic right hemisphere advantages emerging later as configural processing begins to dominate face processing. Thus although hemispheric asymmetry may be present from birth, the behavioural manifestations of such asymmetry may change with the emergence and dissolution of different cognitive abilities and strategies.

There is a substantial amount of evidence that suggests different patterns of spatial impairments are associated with left and right hemisphere injury in adults (Fink et al 2003, Jager and Postma 2003, Martinez 1997, Corballis 1997, Harris et al 2003). Although side specific deficits are more frequent and severe in adults, several authors provide evidence for subtle, persistent deficits in children that differ according to the side of the lesion (Witelson 1987, Stiles 1997). It is of note that the majority of studies are focused on linguistic outcome, but a small number of studies provide evidence of side specific deficits in visuospatial functions. Face processing impairments have been noted in children with right hemisphere lesions (Chiang et al 2000 but see Jones and Tranel 2001) or disruption of input to the right hemisphere (Le Grand 2003). Global and Metric spatial processing can also be disrupted after right hemisphere lesions (Schatz et al 2004). Both left and right hemisphere lesions may cause spatial impairments, but deficits tend to be more severe after right hemisphere lesions (Stiles 1996). Deficits in spatial perception manifest as difficulty defining parts in a spatial array in left sided lesions, whereas right hemisphere patients have problems with configural aspects of the array. Construction tasks reflect similar difficulties, with left hemisphere patients producing simplified constructions, and right hemisphere patients producing configural distortions. Compensatory strategies appeared to improve performance by the age of 6 years, which led Stiles (1997) to advise against immediate interpretation of successful reorganisation of function without first examining the strategies that mediate improvements in performance.

Akshoomoff (2002) examined construction skills in children with early unilateral injury via reproduction of a complex figure. Although performance improved with increasing age, side specific differences were apparent, which indicates that although performance appears to improve, it is compensation as opposed to reorganisation of function that forms the basis of such improvements. Vicari (1998) also found differences between children with left and right hemisphere lesions on a construction task, with right hemisphere patients obtaining lower scores than left hemisphere patients. Patients in these two studies sustained pre or perinatal injuries, which suggests that hemispheric specialisation of function is apparent even around the time of birth. Similar results were obtained by Stiles (1991, 1996), who also emphasises the importance of detailed investigation, so that subtle side specific deficits in spatial function can be revealed. Kolk (2002) also found that children with congenital or acquired right hemisphere lesions performed more poorly on tests of visual and spatial skills. Aram (1988) found that side specific deficits were apparent in children whose injuries were sustained after 2 years of age, with right hemisphere patients obtaining lower Performance IQ scores, which accords with results from Riva and Gazzaniga (1986) studying children with lesions sustained before and after the first year of life. Evidence is mixed regarding IQ scores after unilateral injuries sustained in childhood however, with other studies reporting lower performance IQ scores regardless of hemispheric injury (St James Roberts 1981, Muter 1997).

It is acknowledged that brain injury during childhood appears to result in global cognitive impairment (Hebb 1942, Basser 1962, Milner 1974), which may attenuate detection of side specific impairments. Nevertheless it appears that such impairments may become apparent upon detailed investigation. Although evidence exists for subtle impairments, several authors suggest that impairments in complex aspects of cognitive function after early cerebral lesions do not reflect domain specific deficits per se, but the limits imposed by a general reduction in intellectual function (Bishop 1983, Vargha-Khadem 2001). Confirmation of this suggestion has serious implications for many studies offering support for theories of early specialisation. Further study is needed using IQ matched controls to address the relationship between general intellectual function and patterns of impairment observed on more detailed tests.

Whilst theories of early specialisation receive empirical support, it is difficult to reconcile these theories with the extent of functional recovery observed after unilateral injury in childhood. It is doubtful that equipotentiality or early specialisation can provide a comprehensive account of the spectrum of perceptual and cognitive impairments observed after cerebral insults sustained during childhood. Whilst there are merits to both theories, it seems that an intermediate view would be most suitable in allowing for the possibility of functional overlap between the hemispheres in early childhood, whilst respecting the presence of inherent differences.

1.4.3 Theories of hemispheric specialisation and response to injury 3: Interactive specialisation.

Theories of interactive or ontogenic specialisation are somewhat intermediate between the two contrasting theories outlined above. Unlike the equipotentiality stance, these intermediate views propose that hemispheric specialisation has a genetically prespecified anatomical basis and that structural hemispheric differences manifest very early in life. Unlike the early specialisation stance, the functional expression of these differences are believed to be a product of the interaction between sensory experience and the unfolding architectural blueprint of the developing cerebral hemispheres (Vargha-Khadem 1992, Johnson 2000).

The possibility of interactions between genetics, structural anatomy and cognitive function emphasise the importance of activity dependent development, as suggested in earlier theories of cognitive development (Piaget 1969). The nature of the development of hemispheric specialisation is thus related to differential patterns of input and output in cortical pathways, which subsequently influences their information processing properties. Architectural constraints such as intrinsic connectivity, neurotransmitter concentrations and synaptic density may converge to create such biases. During development, these pathways and structures become increasingly specialised, becoming engaged by a progressively narrower range of stimuli. Consequently, some pathways become more suited to processing certain kinds of input, or processing input in a particular manner. This may occur via synaptic pruning to eliminate inappropriate connections (Jacobs 1999) or redefinition of receptive fields (Safran 1996). These specialised pathways may also be localised within different hemispheres, thus contributing to functional hemispheric asymmetry. Whilst the majority of outcome studies documenting cognitive function after cerebral injuries sustained in childhood are applied to theories of equipotentiality and early specialisation, they are equally applicable to interactive specialisation. Prior to maturation and specialisation of the pathways, the effects of cerebral lesions may be attenuated or even circumvented by compensation from other pathways also responsive to the same types of stimuli. Similarly, residual impairment may relate to failure to re allocate input to an alternative pathway due to prior specialisation of available neural substrates, or deferment to sub optimal pathways. There may also be a global reduction in cognitive function due to lack of available processing space. The interactive nature of functional specialisation of the hemispheres implies that brain injury sustained during development may disrupt the normal pattern of expression of hemispheric specialisation. Several factors may influence the outcome of such lesions, including age at injury (Vargha-Khadem 1997), lesion size (Banich 1990), lesion site (Thal et al 1991), subtle bilateral pathology (Neville 1999), presence of seizures (Muter 1997, Lassonde 2000) particularly status epilepticus (Lothman 1993, Hanhan 2001), the level of development of the cognitive function being studied (Feldman 1992), and age at testing (Stiles 1997).

In summary, each of the three theories of hemispheric specialisation offer an account of possible outcomes after cerebral injuries and their relationship to age at injury. Supporting evidence is provided from studies of patients with cerebral lesions sustained in childhood. A particular difficulty in interpreting results from these studies relates to the use of patients with focal unilateral lesions. A major confound of focal lesions research is that the location and extent of brain damage is often difficult to compare across studies. In addition, intra versus interhemispheric plasticity cannot be separated. Preservation of function may be a result of intrahemispheric compensation or reorganisation of function, or indeed the opposite hemisphere may be responsible for subserving functions normally mediated by the lesioned area. Possible mechanisms include reactivation of functions normally suppressed during lateralised activity by the dominant hemisphere via transcallosal inhibition (Karbe et al 1998), augmentation of systems that may be bilaterally represented (Frackowiak et al 1997) or unmasking of previously inactive pathways (Stephan and Frackowiak 1997). Similarly, if functional impairment is observed, it is difficult to conclude whether the opposite hemisphere is incapable of subserving functions normally mediated by the lesioned area, or whether presence of the damaged region inhibits the opposite hemisphere from mediating a function of which it is entirely capable (de Gelder 1998, Liegeois 2004).

Two patient groups have been particularly valuable with respect to resolving these quandaries. Split brain patients provide an insight into the functional capacity of the isolated left and right hemispheres. Use of unilateral visual field paradigms reveal that certain deficits associated with focal unilateral lesions are not present in these patients such as neglect (Zaidel and Sperry 1981, Plourde and Sperry 1984) and prosopagnosia (Corballis 1998). This implies that damaged regions normally dominant for a particular function may indeed prevent the intact hemisphere from substitution, a phenomena that is silenced by division of the corpus callosum and commissures. Literature documenting function in paediatric patients is extremely sparse, perhaps as a result of the nature of experimental paradigms used to elicit functional profiles of the isolated hemispheres. Stimulus exposure is usually very brief, and rigorous eye movement control is needed, which impose constraints that are often unsuitable if patients have a degree of cognitive impairment.

Another patient group that provides an insight into the function of the isolated left and right hemispheres are hemispherectomised patients. These patients often have intractable epilepsy during childhood and removal of the hemisphere may occur within the first few months of life or even in adulthood. Seizures usually cease or are greatly improved after the procedure, enabling the intact hemisphere to develop and function without the presence of seizure activity. As stimulus exposure and eye movement control are not a particular concern in these patients unless investigating the cortically blind visual field, these patients provide a unique opportunity to investigate the inherent capabilities of the isolated left and right hemispheres.

1.5 Intractable epilepsy syndromes and hemispherectomy

Epilepsy may be regarded as a complex of progressive neurological impairment comprised of seizures, cognitive arrest and regression that may be global or selective, psychiatric disturbances, and motor impairment that manifests as apraxia, dystonia or ataxia. Although plasticity and reorganisation after injury is often discussed in terms of structural lesions, epileptiform activity may represent a physiological lesion in the form of extreme atypical stimulation that also provides an impetus for neural plasticity (Elger et al 2004). Seizures may prevent pruning of immature connections, thus perpetuating synaptic exuberance and increasing the flexibility of the system at the cost of preservation of aberrant connectivity that may adversely affect cognitive development (Jacobs 2000). It makes intuitive sense therefore that seizure activity during the first year of life is especially detrimental to subsequent development. Seizures may have deleterious effects on the construction of elementary frameworks for receiving and responding to input that creates an aberrant foundation for later hemispheric development. Indeed, early age at seizure onset is generally associated with poor cognitive outcome (Hermann et al 2002, Lespinet et al 2002). This accords with evidence from animal studies and human research that illustrates the neurotoxic effects of chronic seizure activity including neuronal loss, metabolic changes and morphological changes visible on MRI. It is also possible that seizure onset later in childhood may impair or eliminate previously integrated cortical functions (Hermann et al 1995). In this manner, the interaction between age at seizure onset and cognitive outcome resembles the effects of structural lesions, with severe global cognitive impairments being evident for early seizure onset, and material specific deficits being evident when seizures occur later during development (Neville 1999, Lassonde et al 2000). Although domain specific impairments are observed in these patients, only temporal lobe epilepsy cases appear to demonstrate hemisphere specific effects. Left temporal lobe epilepsy has been associated with verbal memory deficits (Hermann et al 1997). Right temporal lobe epilepsy has been associated with deficits in spatial memory (Breier et al 1996), famous face recognition (Glosser et al 2003), and identification of emotional expressions (Meletti 2003). Frontal lobe epilepsy in children has been associated with poor attentional and executive function regardless of whether the seizure focus is within the left or right hemisphere (Riva et al 2002, Hernandez et al 2003). Overall, there is a dearth of literature on cognitive profiles of extra-temporal lobe epilepsy. Inconsistencies between tests used and limited coverage of different cognitive aspects of cognitive function contribute to current lack of consensus regarding domain specific impairments in these patients.

Although the effects of epilepsy may be reversible with adequate seizure control, seizures associated with large or multifocal structural lesions are often refractory to medical treatment and warrant surgical procedures. Structural lesions associated with hemispherectomy may be categorised as dysplastic, neoplastic, ischaemic, traumatic, and inflammatory/infectious (Jahan 1997). As neoplastic conditions are mostly relevant to adult hemispherectomised cases and there are no patients within this category in the present study group, it will be omitted from this section.

1.5.1 Cortical dysplasia

The elaborate choreography of cortical development can fail at several different stages of proliferation, differentiation, migration and pruning, resulting in a variety of dysplastic conditions. Hemimegalencephaly is the most relevant example to hemispherectomy studies, and was first described by Sims in 1835. It is a rare developmental disorder characterised by cortical and sometimes cranial and corporeal hemihypertrophy, intractable seizures and psychomotor delay. Milder forms of the disorder affect just one part of a particular lobe, whilst more severe forms involve the entire hemisphere (Taha 1994).

Pathology reports typically describe an enlarged hemisphere (Bignami 1964), with macroscopic features including thickened cortex (King 1985), gyral abnormalities (Laurence 1964, Fitz 1978, Manz 1979) and loss of the grey-white matter interface may be observed (Townsend 1975, Fitz 1978). Occasional preservation of some cortical areas may be preserved (Renowden 1994). Microscopic studies reveal cytoarchitectonic alterations consistent with disorders of neuronal migration, proliferation and differentiation. Polymicrogyria and multifocal heterotopias are frequently observed (Laurence 1964, Townsend 1975, King 1985,), along with loss of hexalaminar cellular layering (King 1985, Farrell 1992, Vigevano 1989), neuronal cytomegaly and abnormal polarity (Fitz 1978, King 1985, Jahan 1997), poor myelination (Vigevano 1989) and varying degrees of gliosis.

Minor dysplastic changes in the intact hemisphere (disruption of laminar architecture and neuronal ectopias in white matter) have been observed (Robain 1989, Jahan 1997), along with autonomous interictal epileptiform activity and progressive encephalopathic changes (Carreno 2001), though these findings are not always regarded a contraindication to surgery (Taha 1994). Outcome after surgery is variable and may be related to incomplete disconnection of fronto-basal structures enabling persistent seizure activity (Carreno 2001,) or abnormalities within the remaining hemisphere as outlined above. Early surgery is associated with better prognosis in these patients (Humbertclaude 1997, di Rocco 2000). Aside from developmental cortical dysplasias that occur as an intrinsic fault in cortical modelling during gestation, there are also acquired dysplasias that result from vascular, traumatic or inflammatory processes.

1.5.2 Vascular insults in the developing brain

The common factor in all ischaemic conditions leading to hemispherectomy is the production of large or multifocal areas of necrosis in one cerebral hemisphere. The precise impact of such lesions on the developing infant brain remains to be clarified. Compromise of the cerebral circulation may create a volume of necrotic tissue due to hypoxia or anoxia. There is a vast system of collateral blood vessels that serve to protect the brain from such insults, but perfusion failure from a major artery can have devastating consequences. White matter in the developing brain is particularly susceptible due to its rapid growth, active metabolic rate and increasing distance from its vascular supply. Development of surrounding regions involves redefining projection pathways to circumvent the necrotic area, leading to acquired cortical dysplasias. Sturge-Weber syndrome and infarcts of a major cerebral artery are the two most common examples of vascular pathophysiology associated with intractable epilepsy and hemispherectomy.

Sturge-Weber Syndrome (SWS) is a neurocutaneous syndrome that results from abnormal development of the embryonic ectoderm. The mutual involvement of the skin and central nervous system reflect their common embryonic origin. The syndrome was first clinically demonstrated by Sturge in 1879. The patient had epilepsy, which had begun in the first year of life, a unilateral facial naevus and glaucoma. He suggested that the epileptiform disorder was caused by a naevoid condition similar to that seen on the patient's face. Indeed, the leptomeningeal angiomatosis (a plexus of densely packed, dilated, tortuous meningeal veins and capillaries) was demonstrated by Kalischer (1901) in post mortem.

Whilst the abnormal venous plexus does not encroach upon cerebral tissue, the excessive perfusion demands of the angioma results in the underlying neural tissue becoming ischaemic and gliotic with premature calcifications (Weber 1922, Krabbe 1934). Occasional reports of cortical dysplasia also exist (Nellhaus 1967, Simonati 1994) which accords with angioma formation preceding the completion of neuronal migratory processes. Both cerebral hemispheres are involved in 15 percent of cases (Boltshauser 1976). Motor and cognitive development proceeds normally until sudden onset of seizures, which result in cortical laminar necrosis, along with hippocampal and cerebellar atrophy. The epileptic focus is often occipito-parietal due to the predilection of the angiomatosis for this area (Hoffmann 1979). There is a transient post ictal hemiparesis that gradually worsens with time, resembling a pyramidal tract lesion. In the malignant form of SWS, seizures become increasingly resistant to medication, and motor and cognitive integrity begin to decline. Early surgery is associated with positive outcome in these cases (Villemure and Rasmussen 1993, Peacock 1995).

1.5.3 Encephalitis

The third major example of pathophysiology that may result in intractable epilepsy is encephalitis. Rasmussen's encephalitis (RE) is the most prominent unilateral sub type relevant to hemispherectomy (Rasmussen 1958). It is a progressive childhood disease usually emerging between 2-10 years of age, peaking at 6 years (Vining 1990) characterized by intractable focal motor seizures, followed by epilepsia partialis continua, progressive hemiplegia and cognitive impairment (Vining 1993, Koehn 1999). Classic signs of inflammation such as perivascular cuffing, astrogliosis, microglial nodules and neuronophagia are present, alongside laminar necrosis, spongy degeneration and blurring of grey and white matter boundaries (Honavar 1992). While one mechanism underlying the pathogenesis of RE has been suggested; the production of excitotoxic GluR3 autoantibodies to the AMPA receptor of the neurone (Rogers 1994), other neuropathological aetiologies have also been indicated. The reduced functional efficacy and altered pharmacology of neuronal Gamma Amino Butyric Acid (GABA) (A) receptors is consistent with overall disinhibition in RE neurons, and could contribute to the generation of the severe epileptic activity evident in this disorder (Gibbs 1998).

Development proceeds normally until seizure onset, which almost always precedes hemiparesis. Cognitive arrest or regression becomes apparent, the disease following a progressive course before stabilising. Bilateral involvement is observed in approximately 5 percent of cases (Andermann 1991). In contrast to the two conditions described previously, debate exists as to whether early surgery is beneficial in these patients, as some groups recommend delay of hemispherectomy to increase the likelihood of successful reorganisation of language (Peacock 1995) whilst others advocate early surgery to circumvent the effects of progressive disease (Villemure and Rasmussen 1993). Reorganisation of function is often clinically evident as a switch in hand preference, and decrease in aphasic symptoms.

In most of the conditions leading to large or multifocal unilateral lesions and intractable epilepsy, treatment options are limited, and consist of medical management, including somewhat experimental and ineffective use of anti epileptic drugs, intravenous antiviral agents or immunosuppressive agents; or surgical resection of the affected hemisphere. The latter option appears to produce the best results with regards to seizure control, and in this respect, hemispherectomy is superior to focal resections (Sugimoto 1999) and callosotomy (Tinuper 1988, Andermann 1992).

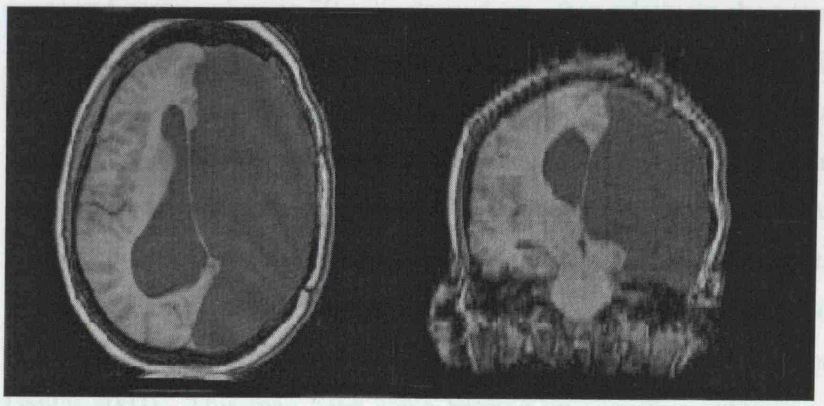
1.5.4 History and development of techniques for hemispherectomy

Surgical removal of a cerebral hemisphere was first reported independently by Dandy and Lhermitte in 1928 as a method of glioma resection in the adult. The first hemispherectomy for intractable epilepsy as a result of infantile brain injury was carried out by McKenzie (1938) and a comprehensive set of cases were subsequently presented by Krynauw (1950) and Ueki (1966).

In the original anatomical hemispherectomy procedure, the anterior, medial and posterior cerebral arteries are clipped to ensure adequate control of haemostasis when removing the diseased hemisphere, and to reduce the volume of the hemisphere, which facilitates the resection process. Bridging veins between the superior sagittal and transverse sinus are also divided. The hemisphere may be removed en bloc or in 4 quadrants that are divided from the lateral ventricle (Carson 2000). Variable portions of the ipsilateral basal ganglia are removed, though debate exists as to the functional significance of preserving these structures (Krynauw 1950, Goodman 1986, Villemure 1992).

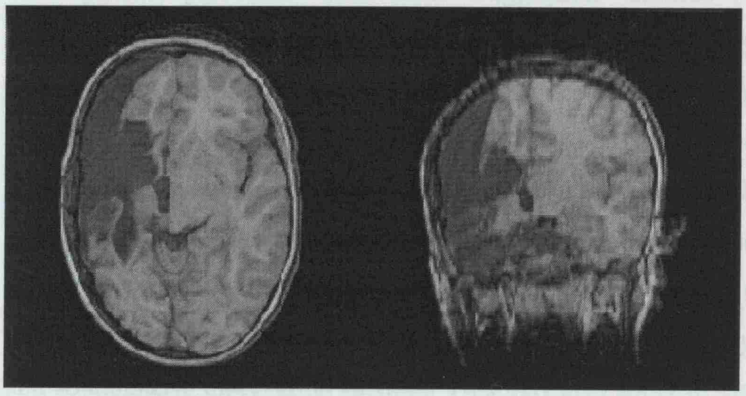
Delayed fatal complications between 1-20 years after surgery in up to 35 percent of patients resulted in the procedure falling out of favour until modifications by Adams (1983) and Rasmussen (1983). The lone hemisphere had no structural support and was vulnerable to haemorrhage and subsequent neurotoxicity from haemosiderosis and hydrocephalus as a result of granular ependymitis (Oppenheimer and Griffith 1966, Hughes and Oppenheimer 1969, Falconer and Wilson 1969). Adams (1983) modified the original hemispherectomy procedure to reduce the volume of the subdural cavity by dural plication to the falx, tentorium and floor of anterior and middle cranial fossae (figure 1.7). The superior sagittal sinus was isolated from the ventricular system by obstructing the foramen of Munro with a plug of muscle.

Figure 1:7. Anatomical hemispherectomy cavity (case **KD** $_{\mathbf{R}}$**8**)



Rasmussen (1983) took a different approach to providing support for the lone hemisphere. In the functional hemispherectomy procedure, the posterior part of the frontal lobe is resected just anterior to the genu of the corpus callosum. The anterior parietal lobe is also resected to the level of the splenium of the corpus callosum. The remaining parts of the frontal lobe are disconnected from the brainstem via sectioning of white matter in front of the rostrum of the corpus callosum to the medial parasagittal pia and along floor of the anterior fossa. The parieto occipital pole is disconnected via white matter sectioning behind the splenium of the corpus callosum and down to falx and tentorium. A temporal lobectomy is then performed, including resection of the amygdala and hippocampus. The remaining frontal and parieto-occipital tissue is thus non functional but vascular, and provides a buttress for the remaining hemisphere (Figure 1.8). Post-operative mortality dropped significantly after the Adams and Rasmussen modifications, and the procedures are now an integral part of epilepsy surgery centres across the globe. There are numerous outcome studies that document seizure control, neurological, motor and cognitive integrity after surgery.

Figure 1:8. Functional hemispherectomy cavity (case **LO$_{L}$8**)



1.5.5 Seizure control

A wealth of reports claim that approximately 70-80% of hemispherectomised patients are seizure free (Wilson 1970, Beardsworth and Adams 1988, Villemure and Rasmussen 1993, Peacock 1996, Doring 1999, Van Veelen 2001, Bittar 2002). These reports have included single cases and studies of up to 70 patients, and are often relatively short term follow ups spanning 1-5 years. Doring (1999) cautions that longer term follow ups are not quite as promising, as although patients with acquired insults were still at 77% seizure free, only 47% of patients were seizure free if they originally suffered a congenital insult. This is similar to long term results reported by Davies (1993), Vining (1997), Maehara (2002) and Devlin (2003), though seizures were markedly reduced and less severe if not absent in most patients. There appears to be a consensus that aetiology has some bearing on seizure control, with developmental dysplastic lesions having the worst prognosis (Carson 1996, Lassonde 2000, Vining 1997, Rintahaka 1993, Devlin 2003). This may have some bearing on cognitive outcome as this patient group also demonstrates more severe cognitive impairment than patients with vascular or encephalitic pathology (Jonas et al 2004, Pulsifer 2004).

1.5.6 Motor outcome

Hemispherectomised patients are often hemiparetic before surgery, demonstrating an increasing proximo-distal gradient of limb paralysis (White 1961), which is most pronounced in the upper limb. Motor impairments rarely increase in severity after the procedure (Wilson 1970, Tinuper 1988, Vining 1997) and some patients demonstrate slight improvements (Krynauw 1950, White 1961, Ignelzi and Bucy 1968, Vining 1997, Devlin 2003). Most patients whose pathology occurred during childhood are ambulant and can run and climb stairs (Griffith 1967, Beardsworth and Adams 1988, Duchowny 1998). The cortical representation of the ipsilateral limb appears to be represented in secondary rather than primary motor cortex (Axel-Muller 1997, Shimizu 2000, Holloway 2000, de Bode et al 2005) and may reflect reorganisation of function or preservation of early pathways that are normally eliminated or inhibited as development proceeds. The latter suggestion accords with early reports of adult hemispherectomised patients that were ambulatory after surgery (O'Brien 1936, Gardner 1933, Bell and Karnosh 1949), though it is acknowledged that some patients did not regain function of the lower limb after surgery (Dandy 1928, Crockett 1951). Spiller (1932) provided an elegant explanation for the preservation of ambulation and the observed proximo-distal gradient of limb paresis following hemispherectomy. He proposed that bihemispheric innervation of the proximal muscles of the lower limb accords with synchronized use of these muscles in standing and walking, whereas more distally situated muscles are employed in more isolated movements and so unilateral innervation suffices. This may also apply to the relatively dense hemiparesis of the upper limb after hemispherectomy, as the upper limbs are less likely to be engaged in bilateral synchronous movements.

1.5.7 General intelligence measures

With regards to cognitive development after surgery, factors that are associated with a good prognosis include preoperative IQ within the normal range and absence of bilateral pathology (Maehara 2002, Rasmussen 1989). The aetiology of the lesion may also be related to outcome (Doring 1999), with cases of developmental dysplasia having the worst prognosis (Curtiss et al 2001, Pulsifer 2004). This may be related to the timing of the insult, as aberrant neuronal migration observed in developmental dysplasias may have more adverse consequences than acquired dysplasias emerging during periods of dendritic and synaptic proliferation. Both Verbal and performance IQ remain relatively stable post operatively, (Vining 1997, Devlin 2003) with modest improvement in some cases. A handful of cases have cognitive profiles within the average range (Damasio 1975, Byrne 1987, Sergent and Villemure 1989, Battro 2000, Vanlancker 2004), but often there is general intellectual impairment across verbal and non verbal domains (Stark et al 1995, Pulsifer et al 2004). Numerous case studies have attempted to elicit more detailed descriptions of the spectrum of ability and impairment in hemispherectomised patients, and the general consensus is that there is often very little difference between left and right hemispherectomised patients on IQ measures (Ueki 1966, Kohn and Dennis 1974, Verity 1982, Strauss and Verity 1983, Ogden 1988, Vargha-Khadem 1991), and that language may be spared at the expense of visuospatial skills (Verity 1982, Battaglia 1999, Mariotti 1998, Gott 1973). Griffith (1966) assumed that cognitive decline occurred with advancing age in hemispherectomised patients, as IQ scores decreased with age. It is possible, and perhaps more likely that the isolated hemisphere reaches a plateau of cognitive ability that subsequently becomes apparent as measurements of intellectual ability become more complex. He further suggests that lateralised differences on the Wechsler scales become more apparent as IQ levels increase. This implies that possible differences may be masked by generic reduction in cognitive function, a suggestion that is evident in other hemispherectomy outcome studies (Gardner 1955, Smith and Sugar 1975).

The possibility of more detailed assessments providing a realistic impression of cognitive outcome was alluded to very shortly after the first series of hemispherectomy outcome studies had been published (Spiller 1932). More specifically, Wilson (1970) argued that IQ measurements may not be an accurate reflection of the spectrum of cognitive impairments in hemispherectomised patients, with more detailed assessments of different cognitive domains being able to elicit often subtle limitations of the lone hemisphere. Indeed, subsequent studies that employed more detailed assessments of particular domains of cognitive function provided a more complete description of the spectrum of cognitive impairments evident after left and right hemispherectomy, particularly with regards to linguistic function.

1.5.8 Linguistic function after hemispherectomy

There is a wealth of literature on reorganisation of language function after left hemispherectomy. There appears to be a general consensus that the isolated right hemisphere is capable of at least some aspects of linguistic function in patients with previously left hemisphere dominant language (Boatman 1999). There is some association between limits of reorganisation and age at onset of pathology, with adult onset left hemisphere disease resulting in global aphasia that persists after hemispherectomy (Zollinger 1933, French 1955, Burklund and Smith 1977). These cases contrast sharply with right hemispherectomised cases for adult onset disease, in which linguistic functions were intact (Rowe 1937, O'Brien 1936), though formal assessments of language were not reported. Aphasic symptoms were also noted in cases where left hemisphere gliomas were diagnosed at 14 years of age (Hillier 1954) and 12 years of age (Gott 1973). Follow up periods were often relatively short due to recurrence of gliomas, and it seems possible that aetiological factors may be involved as 2 case reports of left hemisphere

Rasmussen's encephalitis with seizure onset at 11 (Telfeian 2002) and 13.9 years of age (Boatman 1999) demonstrated marked recovery of speech after surgery.

Several authors (White 1961, Ameli 1980, Basser 1962, Curtiss and De Bode 1999, 2001) propose that there is no relationship between side of hemispheric removal and linguistic outcome if pathology occurs early in life. Indeed, language may be adversely affected by disease of the left or right hemisphere and often recovers to some degree regardless of side of hemispheric removal, which accords with suggests that language is more diffusely represented in the developing brain (see section 1.4). There have been several estimates of the window of time in which recovery of linguistic function may occur after left hemisphere disease and subsequent hemispherectomy. Such estimates range from 10 years of age (Perlstein and Sugar 1954), 5 years of age (Obrador 1964, Vargha-Khadem 1997) to 3 years of age (Liegeois, in press). Although persistent aphasia is extremely rare after left hemispherectomy in childhood, the lone right hemisphere appears to have some limitations with respect to the development of more complex, subtle aspects of language function and phonological processing (Dennis 1975, Stark and Mc Gregor 1997, Ogden 1996). Evidence is mixed, as some authors report age appropriate linguistic abilities after left hemispherectomy that include success on more complex measures such as syntactic comprehension (Marriotti 1998, Curtiss and de Bode 2001). Bishop (1983) argues that subtle linguistic deficits observed after left hemispherectomy might be a result of generic reduction of intellectual abilities, but Marriotti (1998) and Stark and Mc Gregor (1995) found that left hemispherectomised patients demonstrate linguistic deficits that are below that expected for their intelligence quotient. Further study using appropriate control groups matched for intelligence quotient may shed some light on the effects of generic reduction in cognitive impairment on linguistic competence. The issue of control group selection for hemispherectomised patients is addressed in chapter 2 (see section 2.1.2).

1.5.9 Visual cognitive outcome after hemispherectomy

There is a relative shortage of reports with respect to visuo spatial function after hemispherectomy. An important preliminary observation is that almost all patients have homonymous hemianopia that may or may not be accompanied by sparing of the macula region (Rowe 1937, white 1961, Gott 1973, Damasio 1975, Sergent and Villemure 1989). These findings are absolute and bear no relation to age at onset of pathology or age at surgery. Patients do not tend to be acutely aware of the visual field loss, nor does it seem to be a significant source of disability in everyday life (Hendrick 1969, Verity 1982, Wilson 1970).

Both left and right hemispherectomised cases are of interest with respect to assessment of visual cognitive function, as damage to either hemisphere has been related to visuospatial deficits as a result of crowding after left hemisphere disease, and loss of specialised processing after right hemisphere disease. Early reports of hemispherectomy after adult onset disease claimed that no obvious impairments were observed after right hemispherectomy (Dandy 1928, Rowe 1937, O'Brien 1936, though only one study included formal assessment of intelligence (Rowe 1937), and separate results were not provided for verbal and performance IQ. Another case study of adult onset right hemisphere disease and subsequent hemispherectomy (Bell and Karnosh 1949) reported evidence of "some mental retardation" in the immediate post operative period (page 290), though no formal assessments were carried out, and no further references were made in the description of outcome 10 years after surgery.

Subsequent reports including formal assessments of intelligence suggest that performance IQ is usually superior to verbal IQ after late onset of left hemisphere disease and vice versa (Smith 1968), though exceptions exist (Beardsworth and Adams 1988). There is often no difference between the two measures regardless of side of hemispheric removal as mentioned previously, and when a discrepancy is present it usually favours verbal IQ (St James-Roberts 1981). It is possible that performance IQ may be an inadequate measure of visual cognition in hemispherectomised patients due to the motor loading of the subtests. The question of specificity of performance IQ measures for right hemisphere function must also be addressed (Kaufman 1994). Unfortunately, few studies to date have included formal assessments of at least some aspects of visual cognition above and beyond performance IQ. These studies include a large sample of 71 hemispherectomised patients (Pulsifer et al 2004), 7 single case reports (Damasio 1975, Smith and Sugar 1975, Sergent and Villemure 1989, Vargha-Khadem 1997, Marriotti 1998, Vanlancker 2004, Chiricozzi 2005), 6 comparisons of left and right hemispherectomised patients where n = 2-8 (Smith 1969, Gott 1973, Kohn and Dennis 1974, Spencer-Day 1979, Strauss and Verity 1983, Hausmann 2003), and a study of 2 left hemispherectomised patients (Ogden 1988, 1989).

Smith (1968) reports findings from 1 left and 3 right hemispherectomised patients with adult onset of pathology. In addition to verbal-performance IQ discrepancies in favour of verbal IQ, the right hemispherectomised patients also had difficulty with tests of visual short term memory, design copying and abstract non- verbal reasoning. Although not formally assessed, there were no reports of prosopagnosic type symptoms. Left hemispherectomised patient EC demonstrated a VIQ-PIQ discrepancy in the opposite direction, and performance was within the normal range on each of the assessments of visual cognition. In a similar study comparing one left and one right hemispherectomised patient with early onset of disease to a right hemispherectomised case of adult onset, Gott (1973) found that Performance IQ was significantly lower than verbal IQ in the two right hemispherectomised patients. Disparity between verbal and non verbal assessments was greatest in the adult onset case, whereas the paediatric cases demonstrated general reduction in both verbal and non verbal functions.

Other studies of visual cognition after hemispherectomy did not include adult onset cases. Three single case studies report age appropriate performance IQ and integrity of visual cognitive abilities after hemispherectomy. Construction skills, spatial processing, and face recognition were age appropriate 14 years after right hemispherectomy (Damasio 1975) and visual short term memory and construction ability were preserved 21 years after left hemispherectomy (Smith and Sugar 1975). Follow up of the latter case 19 years later (Vanlancker 2004) revealed age appropriate performance on measures of visual closure and face recognition. It is possible that these cases demonstrated intact visual cognitive abilities due to preserved general intellectual function. This is supported by the fact some of the patients in the remaining studies documenting impairments in visual cognitive function also have generic reduction in intellectual function. It is also of note however that none of the case studies described above used a detailed battery of visual cognitive assessments, thus subtle impairments in visual cognition may have remained undisclosed. This is exemplified by studies using different tasks that reveal impaired performance on measures of visual cognition in the context of intact verbal and performance IQ (Ogden 1988, Sergent and Villemure 1989, Marriotti 1998). This highlights the necessity for a detailed battery of assessments to gain an impression of the overall spectrum of visual cognitive abilities following hemispherectomy.

Several authors demonstrated impaired visual cognitive function regardless of side of hemispheric removal (Spencer-Day 1979, Strauss and Verity 1983) including a large sample of 71 patients (Pulsifer et al 2004), though differences existed between the types of impairments observed in the two smaller studies. Spencer-Day (1979) found that left hemispherectomised patient SD (aged 12 years) demonstrated impaired visual memory, visual closure, and produced simplistic drawings. Right hemispherectomised patient DP (aged 6 years 6 months) had a verbal-performance IQ discrepancy in favour of the former, and had difficulty with visual closure and producing spatially coherent drawings. Shortcomings to this study include different assessments being used for each patient, the presence of residual seizures in case SD and different ages at assessment. Differences between errors on constructional tasks were also noted by Strauss and Verity (1983) in their sample of 4 patients. Although left and right hemispherectomised patients both had difficulty with verbal and performance IQ subtests and face processing tasks, drawings of left hemispherectomised patients maintained 3 dimensional structure but lacked details, whereas 3 dimensional perspective was lost in drawings from right hemispherectomised patients. Vargha-Khadem (1997) also noted simplified drawings in left hemispherectomised case Alex, with scores on visual perception and visual motor integration being poor compared to scores obtained on tests of linguistic function. Pulsifer (2004) reports impaired visuomotor integration scores that are consistent with IQ scores. She does not provide detailed analysis of drawings so further conclusions cannot be drawn from this large cohort of left and right hemispherectomised patients regarding constructional function. Collectively, results from these studies suggest that there is a degree of functional overlap between the left and right hemispheres, but subtle differences may exist and become apparent after cerebral injury when assessments are conducted with sufficient detail.

Kohn and Dennis (1974) argued that simple aspects of visuospatial cognition could be mediated by either hemisphere in isolation, but that more complex tasks would reveal limitations in the isolated left hemisphere. 4 left and 4 right hemispherectomised patients with congenital onset of disease were included in this study. Although both groups performed well on simple spatial tests such as personal orientation, right hemispherectomised patients were impaired on more complex measures of spatial ability such as extrapersonal orientation and maze routefinding. The authors concluded that maturation of spatial abilities in the isolated left hemisphere were limited to that of a child aged 10:0, whereas similar abilities in the right hemisphere may mature to at least 15 years of age. Case studies described earlier (Damasio 1975, Sergent and Villemure 1989, Vanlancker 2004) are at odds with this claim, though it is acknowledged that they are isolated examples and different assessment batteries were used. Ogden (1988, 1989) constructed a similar argument for basic components of visual cognition being preserved after hemispherectomy, though she argues that the right hemisphere is also limited in spatial ability due to reorganisation of linguistic functions. Left hemispherectomised patients KOF and JSY demonstrated constructional apraxia for 3 dimensional and complex two-dimensional figures, poor visual recall memory, mild right hemineglect when cancellation tasks involved random arrays, and manipulospatial impairments including mental rotation and judgment of extrapersonal spatial relations. Ogden suggests neither hemisphere in isolation can develop efficient non verbal memory, complex extrapersonal orientation, or higher cognitive visuospatial skills.

It is difficult to reconcile results from different studies, as samples sizes are often extremely small, different tests were used, and patient groups differ according to age at test and age at onset of pathology. There is also a paucity of available literature. It seems that visuospatial functions may be compromised after removal of either hemisphere, and impairments are most evident on relatively complex tasks. Whether this represents an epiphenomenon of generic reduction in cognitive function or specific compromise of visuospatial cognition in the lone hemisphere remains to be elucidated. Two case reports are particularly interesting with respect to this question, as both cases obtained verbal and performance IQ scores approximating the average range, yet performance on certain visuospatial tasks is well below that expected from IQ measures.

Left hemispherectomised case MP was tested 17 years post operatively (Marriotti 1998) aged 20 years. A variety of linguistic and visuospatial tests were administered, and it was apparent that MP had difficulty copying shapes, recognizing objects from unusual views, and computing metric spatial relations. Judgment of line orientation and face processing were also impaired. Whilst MP's performance on linguistic tests were concordant with scores obtained from IQ matched controls, performance on visuospatial tasks was severely impaired relative to controls. It is also of note that almost all of the visuospatial tasks on which MP had difficulty are classically associated with right hemisphere function. Results from this study accord with Ogden's suggestion that visual cognitive ability in the isolated right hemisphere is limited relative to linguistic functions, and appeals to Teuber's crowding hypothesis (Teuber 1975).

Right hemispherectomised case BM is perhaps the most classic case study of visual cognition after hemispherectomy (Sergent and Villemure 1989). BM was assessed 20 years after surgery aged 34, after a chance situation uncovered the presence of dense prosopagnosia of which the patient was completely unaware. Both verbal and performance IQ were within the average range, and performance on construction tasks, mental rotation and extrapersonal orientation were intact. There was also no evidence of neglect or object agnosia. BM had a striking inability to recognise faces. Although gender and age could be extracted from a face without undue difficulty, some difficulties discriminating between negative emotional expressions were observed. Matching different views of the same face proved particularly difficult, in addition to severe impairments recognizing unfamiliar and familiar faces, and no covert knowledge could be elicited. Sergent suggests that onset of cerebral insult at age 5:0 in case BM may have represented a point in development when face recognition was mediated solely by the right hemisphere, and was not sufficiently bilaterally represented to enable recovery of function after removal of the right hemisphere. Removal of the right hemisphere at 13 years of age may have precluded de novo organisation of face recognition in the left hemisphere due to declining plasticity. These suggestions remain to be confirmed in other right hemispherectomised cases. Although BM is the only reported case of prosopagnosia after right hemispherectomy to date, the authors suggest that several other cases may exist but remain undetected due to reliance on non facial cues for recognition and consequent lack of awareness of the deficit.

In summary, it seems that some visuospatial skills may remain immature after hemispherectomy, and debate exists as to whether side specific impairments are observed and if general reductions in cognitive function are related to outcome. There are discrepancies between reports as to which particular skills are intact and impaired, but this may be partly due to small heterogeneous study samples, differences in the types of assessments used, and vastly different time courses of pathology across case studies. Due to the rarity of hemispherectomised patients and the need for novel and more detailed investigations, it is unsurprising that these ideals are seldom met. In general, the initial brain insult and subsequent epilepsy appear to cause some cognitive decline before surgery in the majority of individuals, and this does not appear to change dramatically after surgery. Later onset cases seem to show more lateralised profiles than early onset cases, though it seems there is a general trend across both left and right sided cases for more complex visuospatial skills to be impaired. This would be expected if reorganisation of function proceeds according to an established hierarchy that prioritises language rather than the inherent predisposition of a particular hemisphere for certain cognitive functions. These issues remain to be clarified by studies using larger groups of patients, detailed batteries of visual cognitive assessments, and use of IQ matched controls.

1.6 Summary

The visual system is structurally and functionally complex and is subject to a protracted course of development that extends beyond the first decade of life. Although basic perceptual functions are bilaterally represented in the left and right hemispheres, it remains possible that more complex aspects of visual cognition benefit from relative functional specialisation of the hemispheres. Debate exists as to the extent of hemispheric functional asymmetry, and whether it is apparent during childhood. Evidence from behavioural and clinical studies is mixed, and the majority of clinical studies are confounded by lack of separation between intra and interhemispheric reorganisation or compensation after injury. It is also possible that the damaged hemisphere may inhibit the intact hemisphere from either functional reorganisation or expression of previously established functions that are subordinate but operational in the neurologically intact individual. Callosotomy patients provide an interesting opportunity to study each hemisphere in isolation, but patients often have persistent seizures, and the possibility of transfer of information between the hemispheres via subcortical structures or incomplete disconnection cannot be ruled out. Stringent testing conditions are also needed for these patients to ensure unilateral visual field presentation. Hemispherectomised patients are often free of seizures, and confounding factors related to interhemispheric transfer and eye movement control are absent. These patients therefore provide a unique opportunity to make a detailed assessment of visual cognition in the isolated left and right hemispheres. At present, there is a relative paucity of research dedicated to visual cognitive outcome after hemispherectomy, and most studies are confounded by small sample sizes, a brief range of assessments and lack of IQ matched controls.

1.7 Aims of studies and structure of thesis

1.7.1 Aims of Studies

The aims of the studies described in this thesis were to investigate the integrity of visual perception and cognition in hemispherectomised patients with a view to gaining an understanding of the nature and extent of any limitations observed in the isolated left and right hemispheres. The relationship between side of hemispheric injury and task performance was also addressed, to inform the debate surrounding hemispheric asymmetry of function and subsequent development of function after unilateral cerebral injury. Consideration of the relationship between age at seizure onset on task performance enabled consideration of the validity of different models of the development of hemispheric asymmetry in their application to patients with brain damage sustained in childhood. Use of a control group matched to patients according to age, gender and Performance IQ was used to determine whether visual cognitive function after hemispherectomy reflects specific loss of function or a manifestation of generic reduction in general intellectual function.

1.7.2 Structure of thesis

This thesis is divided into eight chapters. The first two chapters include the background to the studies and details of the subjects involved in this research. The next five chapters are concerned with results from the investigations. Chapters three and four are focused on stereopsis and visual attention. Chapter five is focused on face processing as an example of investigation of ventral stream function, and chapter six is focused on different aspects of spatial processing as an example of investigation of dorsal stream function. Chapter seven is focused on constructional skills, which affords investigation of the interaction between dorsal and ventral streams. The final chapter of this thesis is devoted to a discussion, integrating major findings from each chapter and discussing them in relation to development of lateralised cerebral function, neural plasticity and results from previous hemispherectomy outcome studies. Limitations of the study and possibilities for future research are also discussed in this chapter.

2 Study participants and baseline Neuropsychological assessment

This chapter describes the characteristics (age, gender, verbal and performance IQ) of the study's participants, including the matching process for patients and controls. Baseline neuropsychological measures are included to illustrate the similarities and differences between these groups, and the efficacy of the matching process. The process of data collection and analysis, and the selection criteria are also included.

2.1 Participants

The study population consisted of two principal groups: (a) Hemispherectomised patients and (b) control patients matched with the former group for age, gender and Performance Intelligence Quotient (PIQ). The selection criteria, recruitment literature (see appendices A - C) and proposed studies were approved by the Institute of Child Health and Great Ormond Street Hospital research ethics committee. Written and informed consent was obtained from all parents of all participants, or from the participants themselves if they were aged 16 years or above.

2.1.1 Hemispherectomised patients

2.1.1.1 Selection criteria

Selection criteria for the hemispherectomised patients are summarised in table 2.1. Patients who had undergone complete anatomical or functional hemispherectomy for intractable seizures were selected from a series of 104 children investigated by the epilepsy surgery teams at Great Ormond Street (GOSH) or Kings College Hospitals between 1985-2001. All patients were at least one-year post surgery; this was to avoid possible fluctuations in performance that could be attributed to the acute recovery phase (Boatman 1999, Mittal 2001, Chugani 1994). All children were required to be at least 8 years of age at the time of assessment to ensure sufficient levels of attention and cooperation.

The required level of post-operative seizure control for inclusion to the study was either seizure free or occasional minor seizures (seizures without causing disruption to everyday life), based on the principal categories of the Engel scale (Vining 1997, Carson 2000, Devlin 2003). The presence of unresolved epilepsy reflects damage in the remaining hemisphere, or residual connectivity after functional hemispherectomy, thus introducing a confounding factor in the study of the functional integrity of an isolated hemisphere. It is well established that the presence of seizures has a detrimental effect on neurocognitive function that is above and beyond the effects of the original lesion (Vargha Khadem 1992, Lassonde 2000). In a comprehensive study of 58 patients with uncontrolled temporal lobe epilepsy (TLE) (Hermann et al 2003), cognitive impairment was diffuse and MRI showed morphological changes in extra-temporal sites. Persistent seizure disorders of moderate severity may also require substantial doses of anti-epileptic medication (Neville 1997, Noviasky 2001), many of which are reported to produce side effects such as drowsiness, irritability, blurred vision, ataxia and headaches (Gates 2000). This problem will be revisited in section 2.1.2.2, regarding recruitment of controls.

Table 2.1. Selection criteria for hemispherectomised patients.

Criteria:
At least one year post-surgery
At least 8 years of age
Seizure-free or occasional minor seizures
Binocular acuity greater than 67%
Absence of severe fixation impairments

Near visual acuity impairments were also considered in the selection process. Binocular acuity less than 67% as measured on a one metre Snellen type chart, precluded participation because: (a) Acuity impairments of this level would create difficulties in completing computerized tasks which require resolving details of smaller stimuli (Glaser 1999) and (b) visual acuity impairments reduce the probability of detecting stereopsis (Shah 1995, Menon 1997, Tomac 2001), thus adding a potential confound to results of stereopsis testing in chapter three. Severe fixation impairments and nystagmus as measured by a standard H test of occulomotor function (Glaser 1999, Epstein 2000) also precluded participation in this study, due to obvious difficulties in maintaining focus on test stimuli and performing visual search tasks.

2.1.1.2 Medical and surgical background

Based on the above criteria, a group of 30 patients was selected from a total pool of 104. All 30 patients were contacted and twenty two agreed to participate (see appendix A and B for recruitment information). Twelve of the patients had undergone left hemispherectomy (five anatomical, seven functional) and ten had undergone right hemispherectomy (seven anatomical, three functional). There were 13 males and 9 females in the group, with an age range of 8 years to 24 years 3 months (mean 17: 4). Medical and surgical details of patients are summarised in tables 2.2 and 2.3.

Table 2.2. Medical and surgical background of left hemispherectomised patients (ages in years: months).

Patient	Gender	Age at injury	Aetiology	Age at first seizure	Duration of seizure disorder	Age at surgery	Age at testing
KY$_L$1	Female	Congenital	SWS	0:4	2:8	3:0	11: 3
PO$_L$2	Male	Congenital	SWS	6 days	8:7	8:7	21: 9
RG$_L$3	Male	Congenital	Infarct	2:0	7:7	9:7	18: 3
EBT$_L$4	Female	Congenital	Infarct+ dysgenesis	1:6	12:4	13:10	22: 9
JS$_L$5	Male	Congenital	Infarct	3:0	8:1	11:1	12: 4
HW$_L$6	Female	Congenital	Infarct	7:0	3:4	10:4	24: 3
CB$_L$7	Female	Congenital	Gliosis	0:7	11:9	12:4	18: 7
LO$_L$8	Female	Congenital	Ischaemia	2:0	11:11	13:11	17: 8
NW$_L$9	Female	Acquired 0:18	Infarct	3:6	4:10	8:4	15: 6
PD$_L$10	Male	Acquired 3:7	Rasmussen's	3:7	0:7	4:2	13: 9
TS$_L$11	Female	Acquired 6:0	Rasmussen's	6:6	3:1	9:7	15: 10
JL$_L$12	Male	Acquired 10:0	Rasmussen's	10:0	1:9	11:9	17: 11

Abbreviations - SWS: Sturge-Weber Syndrome, Rasmussen's: Rasmussens Encephalitis, hemimeg: Hemimegalencephaly.

Table 2.3. Medical and surgical background of right hemispherectomised patients (ages in years: months).

Patient	Gender	Age at injury	Aetiology	Age at first seizure	Duration of seizure disorder	Age at surgery	Age at testing
PP$_R$1	Male	Congenital	Hemimeg	4 days	0:4	0:4	11:11
DN$_R$2	Male	Congenital	Hemimeg	0:8	3:4	4:0	11:5
MM$_R$3	Male	Congenital	SWS	0:3	2:3	2:6	8:0
GB$_R$4	Male	Acquired 0:6	Meningitis	7:0	8:6	15:6	19:2
SN$_R$5	Male	Acquired 0:2	Meningitis	2:5	13:7	16:0	20:2
TB$_R$6	Male	Acquired 2:5	Porencephaly	2:5	7:1	9:6	17:2
MS$_R$7	Male	Acquired 4:4	Rasmussen's	4:6	2:6	7:0	18:4
KD$_R$8	Female	Acquired 5:0	Rasmussen's	5:0	4:7	9:7	21:4
BC$_R$9	Male	Acquired 7:0	Rasmussen's	7:0	2:0	9:0	21:2
EBK $_R$10	Female	Acquired 7:0	Rasmussen's	7:0	8:1	15:1	22:6

The spectrum of pathology observed in the hemispherectomised group prior to surgery is representative of the major categories of brain abnormality that predispose an individual to intractable epilepsy as discussed in chapter 1. The relative proportions of each type of aetiology in the study sample are shown in table 2.4. The relative predominance of encephalitic aetiologies is broadly consistent with previous reports (Villemure 1993, Carson 1996, Vining 1997) of clinical outcome after hemispherectomy, yet these cases are the least prevalent according to general admission records at Great Ormond Street Hospital for hemispherectomy candidates.

Table 2.4. Aetiologies of seizure disorders in the study sample.

Aetiology	**Number (& percentage) of patients**
Sturge Weber	3 (13)
Cortical dysplasia	2 (11)
Ischaemic events	8 (36)
Encephalitis	9 (40)

The relatively large number of cases with encephalitic aetiology in this study is a reflection of better prognosis in this group according to cognitive outcome and seizure control (Carson 1996, Doring 1999, Vining 1997) The apparent lack of cases with dysplastic aetiologies within the study group is largely due to a high incidence of bilateral pathology in these cases as evidenced by persistent seizures after hemispherectomy (Doring 1999, Sugimoto 1999, Rintahaka 1993, Carreno 2001, Maehara 2002), and poor cognitive outcome (Curtiss 2001, Battaglia 1999, Devlin 2003, Pulsifer et al 2004) rendering many individuals within this group unsuitable for the current study.

The hemispherectomised patients were divided into 2 sub groups according to side of surgery. These sub groups form the basis of comparisons in later chapters addressing issues of laterality and plasticity. Table 2.5 summarises the details of these two sub groups regarding age at seizure onset, duration of epilepsy pre-surgery, age at surgery and age at the current study. No significant differences between groups were predicted. As all of the variables met parametric criteria, t tests were used to compare group means.

Table 2.5. Summary of hemispherectomised patients with left or right-sided surgery (ages in years: months).

	Left (N = 12)	Right (N = 10)	t
Mean age at seizure onset (range)	3:4 (0:1 – 10:0)	3: 9 (0:1 - 8:0)	t = -.308 p = .761
Interval between seizure onset and surgery (range)	6:5 (0:7 – 12:4)	5:1 (0:4 – 13:7)	t = -.715 p = .483
Mean age at surgery (range)	9:9 (3:0 – 13:11)	8:10 (0:4 – 16:0)	t = -.447 p = .661
Mean age at time of investigation (range)	17:6 (11:3 – 24:3)	17:1 (8:0 – 22:6)	t = -.193 p = . 849
Time elapsed since surgery (range)	7:9 (1:3 – 13:11)	8:3 (3:8 – 12:2)	t = -.334 p = .742

In summary, there were no significant differences between the left and right sub groups for any of the variables tested, thus ruling out basic confounding factors in later analyses that will focus specifically on cognitive function.

The hemispherectomised patients were also divided into groups according to age at initial brain injury. Table 2.6 summarises details in congenital and acquired groups. As only one of the variables did not meet parametric criteria (Age at seizure onset was positively skewed and lepokurtic for the congenital group), t tests were used to compare group means.

Table 2.6. Summary of hemispherectomised patients with congenital and acquired injuries.

	Congenital	Acquired	t
N =	11 (8 L, 3 R)	11 (4 L, 7 R)	
Mean age at seizure onset (range)	1:7 (0:1- 7:0)	5:5 (2:5 – 10:0)	t = -4.008 p = .001**
Interval between seizure onset and surgery (range)	6:5 (0:4 – 12: 4)	5: 1 (0:7 - 13: 7)	t = -.859 p = .400
Mean age at surgery (range)	8:2 (0:4 – 13: 11)	10:6 (4:2 – 1:0)	t = - 1.28 p = .215
Mean age at time of investigation (range)	16:2 (8:0 - 24:3)	18:5 (13:9 - 22:6)	t = -1.22 p = .238
Time elapsed since surgery (range)	8:0 (1:3 – 13:11)	7:11 (3:8 – 12:2)	t = -.083 p = .935

As expected, there was a significant difference between the two groups with respect to age at seizure onset. The result for age at seizure onset was confirmed with non parametric statistics (Mann-Whitney U: Z = -.323, p = .001). The mean age at surgery, duration of seizure disorder prior to surgery and age at test were similar for both groups. Early age at seizure onset has been associated with adverse cognitive outcome in epilepsy patients (Smith 2002, Bulteau 2000, Glosser 1997), specifically performance IQ measures (Jansen 2005, Rodin 1986). Duration of seizure disorder has also been associated with adverse outcome (Dalmagro 2005, Smith 2002, Lee 2001, Bulteau 2000) but debate exists (Glosser 1997).

Tables 2.5 and 2.6 illustrate that although left-right and congenital-acquired sub groups contain relatively equal numbers of patients, there are more left hemispherectomised patients in the congenital group, and more right hemispherectomised patients in the acquired group. This is not a general reflection of the number of patients presenting for left and right hemispherectomy for intractable seizures. Although approximately equal numbers of patients undergo the surgical procedure (Devlin 2003, Vining 1997, Carson 2000, Peacock 1996), the behavioural and cognitive difficulties observed in patients with congenital right-sided injuries (Woods 1980, Nass 1989, Brumback 1982, Neville 1999, Curtiss and de Bode 1999) often precludes their inclusion in neuropsychology studies. Two relevant observations provide reasoning for the apparent paucity of acquired left sided cases in this study. Firstly, there are a greater number of patients with congenital as opposed to acquired brain injuries within the general pool of hemispherectomised patients at Great Ormond Street Hospital (Devlin 2003). As a result, the left hemispherectomised patients selected for this study are more representative of the proportions encountered in the general pool, as there are fewer constraints when selecting patients with congenital left sided injuries as opposed to patients with congenital right sided injuries as mentioned earlier. Secondly, of the left hemispherectomised patients with acquired aetiologies, several patients had obsolete contact details that could not be updated, thus reducing the available patients in this category still further.

When considering factors that may correlate with task performance, it is acknowledged that the source of cognitive impairment in children with epilepsy is probably multifactorial. Unfortunately it is extremely difficult to separate the effects of potentially relevant variables. Firstly, it is difficult to disentangle the effects of epilepsy from the original brain insult. In children with newly diagnosed epilepsy, cognitive function was found to be impaired relative to siblings or controls (Austin et al 2002, Oostrom et al 2003). Conversely, the neurocognitive sequelae of seizures are known to extend above and beyond the effects of the original lesion (Hermann et al 2002). Thus, cognitive impairment in individuals with epilepsy cannot be exclusively attributed to the primary lesions or the course of the seizure disorder. Regarding other factors, inter-ictal activity is difficult to estimate, and actual seizure frequency and severity are often difficult to assess due a proportion of seizures being unwitnessed, particularly at night. In the light of the above and the fact that age at initial onset of pathology cannot always be reliably calculated, the relationship between age at brain injury and task performance was addressed by using age at seizure onset for each of the four subgroups (left hemispherectomy, left control, right hemispherectomy, right control). Age at seizure onset can be more precisely defined than the age at which a brain lesion first appears, it is a variable that is equally applicable to patients and controls, and as discussed earlier, seizures represent a physiological lesion that can obstruct cognitive development (Muter et al 1997, Elger et al 2004). It is therefore of interest to address the crowding hypothesis by predicting that later onset of seizures in the left hemisphere will be associated with better visuospatial skills, as prior establishment of visuospatial skills in the right hemisphere would lead to resistance in accommodating language function, thus negating the effects of crowding.

2.1.1.3 Handedness

Ten of the left hemispherectomised patients were left handed prior to surgery and thus did not change handedness during the course of the seizure disorder or after surgery. Although left handedness is usually prevalent in only 10 % of the general population (Annett 1998), the increased prevalence in the left hemispherectomised patient group was unsurprising in the light of the fact that right hemiparesis was present in the first three months of life in 4 patients and before 9 months of age in another 4 patients, thus introducing bias to the development of hand preference. This finding accords with previous studies of individuals with early left hemisphere lesions, which report a substantial increase in left handedness following such injuries (Vargha-Khadem 1985, Orsini and Satz 1986, Isaacs et al 1996). Debate exists as to when handedness is established, with early signs of consistent preference emerging around 7 months of age (Hildreth 1949, Bishop 1990), with the vast majority of children possessing a clearly dominant hand by 2-3 years of age (Bishop 1990).

Table 2.7. Handedness of hemispherectomised patients in study sample

	Left Hemispherectomy	Right Hemispherectomy
Always left handed	9 (8 cong, 1 acq)	-
Always right handed	-	8 (3 cong, 5 acq)
Switched from left to right	-	2 (2 acq)
Switched from right to left	3 (3 acq)	-

Abbreviations - cong: congenital, acq: acquired.

Of the remaining 4 cases, patient **JL $_L$12** was always left handed and thus did not change handedness when right hemiplegia emerged at 11 years 5 months respectively. Patients **NW $_L$9**, **PD$_L$10** and **TS $_L$11** were originally right handed and subsequently changed handedness during the course of the seizure disorder, with right hemiplegia emerging at 18 months, 3 years 6 months and 6 years of age respectively. Eight of the right hemispherectomised patients were right handed prior to surgery. Four patients had left hemiplegia within the first few months of life and so developed mandatory right handedness. Although another three patients in this group did not have hemiplegia before 18 months of age and so natural dominance was able to develop, it is unsurprising that these patients were right handed given that approximately 90 percent of individuals in the general population are indeed right handed (Annett 1998). Patients **TB $_R$6** and **EBK $_R$10** were originally left handed and subsequently changed handedness during the course of the seizure disorder, with left hemiplegia emerging at 2 years 11 months and 9 years 6 months respectively. Switching of hand preference during the course of the seizure disorder has been previously reported in hemispherectomy studies (Vargha-Khadem and Mishkin 1997), and is sometimes accompanied by transient aphasia. This is thought to reflect changes in linguistic as well as motor hemispheric dominance and was observed in case **PD$_L$10**.

2.1.1.4 Visual problems – optics and everyday life

Information regarding visual problems experienced before surgery and visual-spatial abilities in everyday life was obtained through medical records and a questionnaire sent to the parents of the patients during the recruitment process (appendix C). The questionnaire was designed to elicit information from parents regarding visual disturbances observed before surgery, current visual problems such as strabismus, myopia and hypermetropia, strategies used to overcome hemianopia, reaching and grasping behaviour, motion perception, estimation of distances, sense of direction in the home and local environment, attentional neglect, general object and face recognition abilities and whether the patient had favourite television and film personalities to aid the creation of a famous faces task that will be discussed in chapter 5. The questionnaire proved to be extremely valuable with respect to providing an insight into visual and spatial experience in every day life, and strategies used to overcome hemianopia. The information obtained from the questionnaires was utilised for the creation of a suitable testing environment, and to establish potential difficulties for each patient with regards to the different elements of the assessment phases. Information obtained from medical records and the questionnaire highlighted several abnormal visual phenomena prior to surgery, indicating involvement of the visual system in the course of the seizure disorder. Table 2.8 summarises the main findings. Intermittent exotropia in the eye ipsilateral to the lesion was the most frequent disorder related to surgery. At the time of assessment, 7 patients had intermittent exotropia, which affected the eye ipsilateral to the lesion. 2 patients had undergone corrective surgery for this condition, and 1 patient experienced spontaneous resolution.

Both human and animal studies report degeneration of retinal ganglion cells after hemispherectomy (Stoerig 1996, Azzopardi 2001). Despite this possibility, only 27 percent of patients had a clinical diagnosis of refractive error, with most diagnoses emerging many years after surgery. It is therefore possible that myopia is unrelated to surgery and merely reflects the pattern of changes in the lens that would have occurred naturally. There are currently no published reports on the majority of visual sequelae listed in table 2.8 for hemispherectomised patients, though some earlier studies reported abnormalities in fixation and smooth pursuit (Troost 1972, Estanol 1980 but see Herter 2004).

Table 2.8. Visual phenomena prior to surgery.

Visual disturbance	Number (and percentage of patients) before surgery	Number (and percentage of patients) at follow up
Myopia	1 (4)	6 (22)
Hypermetropia	2 (9)	1 (4)
Exotropia	4 (18)	7 (32)
Photophobia	4 (18)	0
Blurred vision	2 (9)	0
Tunnel vision	2 (9)	1 (4)

There were no reported problems with reaching and grasping behaviour or following moving objects with the eyes. There were also no reported problems with recognising and using everyday objects, and no reported difficulties recognising familiar faces, which will be discussed further in chapter 5. The questionnaire did highlight some difficulties regarding visual behaviour in everyday life, which are summarised in table 2.9. Almost half of the patients in the sample reported that turning the head to the side contralateral to the lesion negated some of the effects of the contralateral homonymous hemianopia. However, colliding with objects and people in the hemianopic field was the main difficulty reported in the questionnaire. Reports of washing on one side of the body indicated motoric difficulties as opposed to attentional neglect, as it is the side ipsilateral to the lesion that is neglected. Additionally, no other phenomena associated with neglect were reported such as leaving food on one half of a plate or leaving drawings half completed. None of the patients reported experiencing profound difficulties as a result of hemianopia, which accords with previous hemispherectomy outcome studies that addressed this question (Hendrick 1969, Verity 1982, Wilson 1970). Visual attention will be explored in chapter 4. Estimating distances between objects and disorientation in the local environment proved difficult for some patients, and this will be addressed in chapters 6, which is focused on spatial processing. Again, there are no published reports at present that document visual and spatial difficulties in everyday life in hemispherectomised patients, and it is acknowledged that the above phenomena reported in this study were not formally tested.

Table 2.9. Aspects of visual behaviour in everyday life

Visual phenomena in everyday life	**Number (percent) of patients**
Compensatory strategies for hemianopia	9 (41)
Colliding with things in hemianopic field	16 (73)
Wash only one side of the body	7 (32)
Problems with distance estimation	8 (36)
Disorientation in local environment	6 (27)

2.1.1.5 Seizure status

Medical records were consulted to obtain information regarding episodes of status epilepticus to gain an impression of seizure generalization to the intact hemisphere, and current seizure status. Both of these variables are known to adversely affect cognitive performance in the developing brain (Singhi 1992, Binnie 1994, Muter 1997).

Table 2.10. Summary of seizure status in the hemispherectomised patient group

Seizure phenomena:	Number and percentage of patients
Episodes of status	6 (27)
Currently seizure free	20 (91)
Currently minor seizures	2 (9)

2.1.1.6 Motor function

All patients were ambulatory. Regarding the function of the hemiparetic upper limb, all patients had some shoulder movement, with a gradient of functional impairment increasing in a proximal – distal direction. Only one of the patients (**HW** $_{L}$**6**) could voluntarily flex or extend the wrist of the hemiparetic limb to assist functional use of the hand, and movement in the fingers was minimal in all patients. Mirror movements were observed in the hemiparetic hand in 3 patients (**EBT** $_{L}$**4**, **JL** $_{L}$**12** and **HW** $_{L}$**6**), and patient **HW** $_{L}$**6** demonstrated voluntary functional grip (Dijkerman 1993), as she was able to spontaneously pick up a variety of objects such as cups and pencils without undue difficulties. The principal visual and motor difficulties associated with hemispherectomy in the sample of patients involved in this study are broadly representative of known visual and motor impairments observed after hemispherectomy in childhood and adolescence. Contralateral homonymous hemianopia and hemiparesis are the main persistent neurological sequelae observed after the procedure both in the general population of hemispherectomised patients presenting to GOSH for post surgical follow up (Holloway 2000, Devlin 2003) as well as other hemispherectomy populations (Peacock 1996, Vining 1993, Kossoff 2002). In most cases, hemiparesis is present before the procedure and there is often minimal change in the severity of paresis after surgery (Hendrick 1969, Tuite 2000).

2.1.1.7 Demographic information

Demographic information pertaining to Housing, education and employment was obtained from parents of the patients during the recruitment process. Table 2.11 summarises the details. Carson (1996) categorised cases according to whether patients were working independently or participating in age appropriate education (independent), working in sheltered employment or attending a special needs school (semi-independent), or needing assistance with basic daily living functions and not participating in education or employment programmes. Wilson (1970) and Lindsay (1987) report similar categories.

Table 2.11. Demographic information for hemispherectomised group.

Demographic variable	**Number (and percentage) of patients**	**Approximate Carson category**
Living independently	3 (13.5)	
Living at home	16 (73)	Dependent 0
Residential	3 (13.5)	
		Semi-
Mainstream school/FE college	4 (18)	Independent 16
Special needs school/FE college	10 (45)	
Employment	3 (14)	Independent 6
University	1 (4)	
Not in employment or education	4 (18)	

The above findings collectively suggest that the sample of patients involved in this study is generally representative of the wider sample of patients presenting to Great Ormond Street Hospital for post surgical neuropsychological follow up after hemispherectomy and are concordant with reports from other centres on hemispherectomised patients with respect to aetiology and general outcome.

2.1.2 The control group

It is currently unresolved whether cognitive profiles observed in hemispherectomised cases are a product of cognising with a single left or right hemisphere or alternatively a result of generic reduction in intellectual ability (see chapter 1, section 1.5). The principal mode of comparison in outcome studies of hemispherectomised patients is a within group design whereby patients are also used as controls. Left hemispherectomised patients are compared to right hemispherectomised patients to explore laterality issues (Gott 1973a, Kohn and Dennis 1974, Verity 1982, Strauss 1983, Vargha-Khadem 1991, Stark 1995). Patients with prenatal injuries are occasionally compared to patients with later injuries to explore plasticity and reorganisation of function (Curtiss et al. 1999, 2001). Whilst these studies provide an interesting comparison between the functional integrity of isolated left and right hemispheres, and those with early and late lesions, there are several shortfalls. Studies are often very small, due to the rarity of the patient group, with some comparisons being made between just two patients (Day 1979), or single case reports are compared with results from previous studies (Menard 2000, Damasio 1975, Sergent 1989, Gott 1973). The matching criteria used in these studies are often minimal, usually resulting in comparisons between patients of different gender, ages and aetiologies. Despite these shortfalls, these case to case comparisons enable a detailed investigation of a particular question without results being dissolved in what would have been two larger but extremely heterogeneous groups.

Even though the above shortcomings have been justified to some degree, a crucial point is that little has been said in previous studies about specific effects of cognising with a single hemisphere. Gott (1973) and Bishop (1983) alluded to the possibility of cognitive profiles observed in hemispherectomised patients reflecting a generic reduction in reasoning ability. The most effective method of investigating the cognitive profile of an isolated hemisphere is to make a comparison with control subjects with two functional hemispheres who are also of the same age, gender, seizure status and a similar level of general reasoning ability. In this manner, potential confounding variables are reduced, impairments in general intellectual function are negated, and remaining differences between patients and controls are more likely to be the result of cognising with a single hemisphere.

2.1.2.1 Rationale for recruitment of Epilepsy control group

The method of recruitment used in this study enables both within and between group comparisons. Hemispherectomised patients with left and right injuries, or early and late onset of seizures will be compared, and additionally, the hemispherectomised patients will be compared to a control group matched for age, gender and Performance Intelligence Quotient (PIQ). Most neuropsychological studies investigating cognitive function after hemispherectomy utilised control groups that were either neurologically intact and thus serving as a baseline (Sergent 1989, Stark 1995, Ogden 1996, de Bode 2000), or patients with left and right hemisphere lesions were compared as mentioned previously, with some studies using both types of comparison. Only two studies to date have utilised data from control subjects matched in IQ to hemispherectomised patients (Bishop 1983, Mariotti 1998). These studies proposed that levels of linguistic function in hemispherectomised patients may be a product of a generic reduction in intellectual abilities, but Marriotti also found that that certain visuospatial abilities were selectively impaired in case MP when compared to IQ matched controls. As Bishop's article was a reappraisal of a previous study utilising data from Dennis and Kohn (1975) and Marriotti reported a single case with left hemispherectomy, no firm conclusions can be drawn. Nevertheless, results on selective impairment of visuospatial skills after hemispherectomy are of interest, and warrant further investigation of hemispherectomised patients, with subsequent comparison to controls.

Curtiss (2001) considers the selection of an appropriate control group for children that have undergone hemispherectomy. She concludes that there is no adequate control group due to confounding factors, but there is no elaboration as to the nature of these factors. It becomes clear that studies investigating the effects of focal unilateral lesions are often able to recruit controls with reasoning ability in the borderline to low average range to match patients (Muter 1997). It is extremely difficult to recruit suitable controls for hemispherectomy studies, given that suitable participants should have two functional cerebral hemispheres but an IQ approximately 2-3 standard deviations (SD) below the mean (mean 100, SD 15). Neurological disease would invariably be suspected at this level of cognitive function, and many individuals with IQ measures at these levels but often without explicit focal lesions fall into syndrome groups such as Downs (Wang 1995, Pinter 2001), Autism (Sandberg 1993, Hill 2003), and Williams (Atkinson 2003, Bellugi 1990). These groups have distinct neurocognitive profiles that would confound results when attempting to make general comparisons with the hemispherectomy group.

Another example of individuals with cognitive impairment but occasionally without distinct neurocognitive profiles is children and adolescents with epilepsy. Indeed, previous studies have advocated the use of a non surgical epilepsy control group for investigating cognitive outcome in patients that have undergone epilepsy surgery (Smith et al 2002). Whilst there are epileptogenic foci within the brain, the two hemispheres have some degree of function interictally. Additionally, there is a diffuse spectrum of neurocognitive sequelae associated with epilepsy (Elger et al 2004), which reduces the probability of an epilepsy control group displaying a uniform profile that would confound certain test results. It is acknowledged that there are obviously unspecified areas of brain injury in these cases as a result of seizure activity and thus it cannot be said that the two hemispheres are completely intact. The same can also be said of the hemispherectomised patients, as the remaining hemisphere endured generalized epileptiform activity in the majority of cases. In this manner, two cerebral hemispheres that *are* intermittently affected by seizure activity (control participants) are being compared to a single hemisphere that *was* intermittently affected by seizure activity (hemispherectomised patients). As the general nature of unspecified injury is the same for both groups (i.e. seizures), and it was possible to access a database of individuals with epilepsy presenting to Great Ormond Street Hospital to select suitable candidates, children and adolescents with epilepsy were chosen as controls for hemispherectomised patients with low IQ.

2.1.2.2 Selection criteria

Control participants were recruited through the epilepsy surgery database at Great Ormond Street Hospital, and contacting further education colleges to find control participants to match hemispherectomised patients with an IQ in the average range. Participants from the Great Ormond Street epilepsy surgery database had undergone investigations to explore the possibility of neurosurgery to relieve seizures, but were subsequently rejected due to the nature of the epileptic foci being unsuitable for resection. Unsuitable foci included diffuse, poorly localised, bilateral and multifocal lesions. The presence of neurological disease in addition to epilepsy, or neurocognitive syndromes such as Autism, Downs Syndrome or Williams syndrome precluded participation in this study. These criteria served to limit the possible causes of the observed cognitive profile during the assessments to the effects of intermittent seizure activity. Participants were matched to a hemispherectomised patient by gender, date of birth within 12 months of the hemispherectomised patient's, and a performance IQ measured within the last 12 months that was within 10 points of that obtained by the hemispherectomised patient within a similar time period. Seizure control was required to be effective enough to enable assessment without significant risk of seizures occurring.

Although side effects from anti epileptic medication may provide additional confounding factors when studying cognitive function as mentioned in section 2.1.1.1, results are mixed. Mandelbaum (1997) examined cognitive ability in 43 children before and after commencement of anticonvulsant medication. Analysis of subjects' performance after 6 and 12 months of antiepileptic therapy showed no significant deterioration attributable to medication. The differences in cognitive performance of the four seizure groups (generalized convulsive, generalized non-convulsive (absence), simple partial, or complex partial seizures) at baseline were not apparent at the time of follow-up. Reviews of studies documenting the adverse effects of antiepileptic medications on behavioural and cognitive function (Dodrill 1991, Gates 2000) concluded that a paucity of recognized and validated methods of assessment has resulted in severe methodological limitations in these studies, a major shortcoming being contamination of drug effects and subject effects. Nevertheless, it must be acknowledged that side effects of medication are a potential confounding factor with respect to performance of control subjects.

The matching process enabled a comparison of individuals of the same age and gender and with similar levels of non verbal reasoning ability. The major difference between the two groups was subsequently reduced to having two functional hemispheres versus a single functional hemisphere, the most obvious manifestation being hemianopia and hemiparesis in the hemispherectomised group. Age and gender matching criteria were included to reduce confounding factors relevant to neuropsychological assessments. Although some standardised neuropsychological tests account for age related changes in performance by providing scaled scores, non standardised tests, experimental tests and those simply without scaled scores would be vulnerable to age related performance and thus difficult to interpret if patients and controls differed significantly in age. There is also some evidence for gender related differences in cognitive function; particularly spatial processing (Quaiser-Pohl 2002, Levine 1999) though controversy exists (Young 1994, Masters 1993). Matching for gender therefore eliminated another potential confound when interpreting results.

2.1.2.3 Details of the control group

Based on the above criteria, a group of 19 control subjects matched individually by age, gender and performance IQ to each of 19 patients, was recruited for these studies. The medical details of the control group are summarized in table 2.12. Difficulties in finding suitable matches for 3 adult male patients (**PO_L2, TB_R6, BC_R9**) precluded complete one to one matching of patients and controls. None of the control subjects had hemianopia, the only reported visual phenomena being myopia in cases **$GB_{CR}1$** and **$GP_{CR}3$**, and moderate deuteranomaly in case **$GB_{CR}1$**. Mild right-sided weakness was reported in case **$BL_{CR}5$**, and timed fine motor co-ordination as measured by the Annett peg sorting task (Annett 1976) was reported to be slower than average in cases **$DD_{CR}6$, $NL_{CL}6$** and **$LW_{CL}10$.** Due to severe difficulties in locating suitable controls according to criteria already described, and the fact that the hemispherectomised patients are mostly mandatory left or right handers, handedness is not included in the matching criteria in this study. It is interesting to note that although none of the control subjects reported any motor difficulties, there is a 3 fold increase in left handedness in this group as compared to the general population (Annett 1998). An increase in left handedness has been consistently observed in groups of individuals with neurocognitive impairments, including epilepsy (Van Strien 1987, Dellatolas 1993).

The questionnaire relating to visual and spatial ability in everyday life was also given to control subjects. There were no reported difficulties. In summary, 19 control subjects were selected who met the matching criteria for this study. The characteristics of patient and control groups are summarized in table 2.13.

Table 2.12. Summary details of control group

Control Code	Gender	Age	Seizure type (Medication + / -)	Hand	Seizure onset	Patient matched
$NM_{CL}1$	Female	12:3	CP +	R	4:0	**KY_L1**
$EG_{CR}4$	Male	18:6	TC +	L	5:0	**RG_L3**
$AS_{CL}3$	Female	23:6		R		**EBT_L4**
$LB_{CL}4$	Male	11:11		L		**JS_L5**
$MP_{CL}5$	Female	25:3	Absences -	R	15:0	**HW_L6**
$NL_{CL}6$	Female	18:3	TC +	R	0:11	**CB_L7**
$VB_{CL}7$	Female	17:8	CP and Absences+	R	1:0	**LO_L8**
$HR_{CL}8$	Female	15:11	Absences +	R	1:6	**NW_L9**
$RC_{CL}9$	Male	13:5	TC +	R	4:0	**PD_L10**
$LW_{CL}10$	Female	16:1	Aura only	R	14:0	**TS_L11**
$EA_{CL}11$	Male	18:11		R		**JL_L12**
$GB_{CR}1$	Male	11:0	CP and TC +	R	3:0	**PP_R1**
$AD_{CR}2$	Male	11:2	Focal motor +	R	3:0	**DN_R2**
$GP_{CR}3$	Male	8:5	TC +	L	0:1	**MM_R3**
$AR_{CL}2$	Male	19:0	TC +	L	7:0	**GB_R4**
$BL_{CR}5$	Male	19:3	CP +	L	5:0	**SN_R5**
$DD_{CR}6$	Male	18:5	CP +	L	0:6	**MS_R7**
$MA_{CR}7$	Female	20:4	CP and TC +	R	7:0	**KD_R8**
$MR_{CR}8$	Female	22:2	Absences -	R	12:0	**EBK_R10**

Abbreviations: CP = complex partial seizures, TC = tonic-clonic seizures, + = medication, - = no medication.

Table 2.13. Group characteristics.

Subject group	**Group size**	**Mean age (+/-SEM)**	**Age range**	**Gender**
HY_L	12	17: 6 (1.167)	11:3 – 24:3	5M, 7F
CT_L	11	17: 5 (1.285)	11:11- 25:3	4M, 7F
HY_R	10	17:1 (1.566)	8:0 – 22:6	8M, 2F
CT_R	8	16:3 (1.820)	8:5 – 22:2	6M, 2F
HY	22	17: 4 (0.932)	8:0- 24:3	13 M, 9 F
CT	19	16:11 (1.048)	8: 5 – 25:3	10 M, 9 F

HY_L = left hemispherectomy group; CT_L = control subjects matched to patients with left hemispherectomy; HY_R = right hemispherectomy group; CT_R = control subjects matched to patients with left hemispherectomy; HY = hemispherectomy group; CT = control group. M = male, F = female.

Gender ratios for each subgroup were well balanced, due to the individual matching process, and each control subject was within the 12 month parameter of age at testing. The mean ages for each sub group were compared to evaluate the efficacy of the matching process between hemispherectomised patients and their controls. As parametric criteria were met, t tests were used. Two tailed t tests did not reveal any significant age differences between hemispherectomy and control groups ($t = .281$, $p = .780$), nor between left hemispherectomised patients and their controls ($t = .027$, $p = .979$), or right hemispherectomised patients and their controls ($t = .375$, $p = .713$). In summary, these results suggest the groups were well matched according to age and gender.

Patients and controls were invited to attend for these studies in two phases. Age matching was based on age at phase one, when the vast majority of data were collected, and all phase two assessments occurred within six months of phase one. The time lapse between phases one and two could have potentially reduced the efficacy of the age matching criteria between patients and controls. To confirm that the age criteria were still met for phase two, further comparisons were made. There were no significant age differences between hemispherectomy and control groups ($t = .644$, $p = .524$), nor between left hemispherectomised cases and their controls ($t = .347$, $p = .732$), or right hemispherectomised case and their controls ($t = .562$, $p = .582$). Almost all cases were still were still within the 12 months matching parameter. Two right hemispherectomy cases were more than 12 months older than their corresponding control subject during phase two (**KD$_{\mathbf{R}}$8** aged 21:10 at phase two is 18 months older than **MA$_{\mathbf{CR}}$7** aged 20:4, and **SN$_{\mathbf{R}}$5** aged 21:8 at phase two is 15 months older than **BL$_{\mathbf{CR}}$5** aged 19:3). As these cases are within an age group where most cognitive functions are well established and subject to minimal age related fluctuations, in addition to the severe limitations in locating control subjects within this age group, the breach in matching criteria was accepted.

2.2 Baseline Assessments

As mentioned previously, neuropsychological data was collected in two phases (appendix D). Phase one entailed two full days of assessment. Phase two occurred within 6 months of phase one, and entailed 1 full day of assessments. All tests were administered in the same order for each participant. Where several tests were used to assess a particular domain of function such as face processing or left-right discrimination, they were interspersed with tests from other domains to reduce practice effects and to reduce the likelihood of the participants becoming disinterested.

2.2.1 Introduction

The results from the Wechsler Scales of Intelligence are presented in this section to provide a general overview of the level of cognitive function within the study sample. Comparisons between patients and controls were made to complete the final stage of the matching process and to explore possible discrepancies between hemispherectomy and control groups on different subtests that may be relevant in related perceptuo-cognitive domains in later chapters. Within group comparisons are also presented for the hemispherectomy group, to explore possible effects of side of hemispheric removal.

There is an abundance of literature on the effects of unilateral lesions sustained in childhood on measures of intelligence. Pertinent findings in larger studies include lower PIQ than VIQ scores in patients with left (Nass 1989) and right hemisphere injury (Riva and Gazzaniga 1986), and lack of VIQ-PIQ discrepancies (Vargha-Khadem 1992, Isaacs 1996). Where discrepancy exists it is usually in favour of VIQ, regardless of side of injury (Muter 1997, Vargha-Khadem 2000). As discussed in chapter 1, several studies reporting post-operative data on hemispherectomised patients for lesions sustained during childhood include IQ measurements. Conclusions regarding VIQ-PIQ discrepancies are mixed. Evidence for early cerebral lateralisation in the form of VIQ-PIQ discrepancies according to side of hemispherectomy is sparse and criteria for discrepancy differ across studies. Only a small selection of case results from the literature suggest verbal IQ is compromised relative to PIQ in patients with left hemispherectomy (Vargha-Khadem 1991, Dennis and Whitaker 1976, Strauss and Verity 1983, Beardsworth 1988). The finding of lower PIQ than VIQ scores in patients with right hemispherectomy is more abundant (Ignelzi and Bucy 1968, Gott 1973, Day and Ulatowska 1979, Vargha-Khadem 1991, Ogden 1996), though PIQ is often lower than VIQ regardless of side of pathology (Gott 1973, Strauss and Verity 1983, Ogden 1989, 1996, Battaglia 1999). Indeed, an extensive review of IQ results from hemispherectomised patients (St James-Roberts 1981) suggests that there appears to be more reports of VIQ scores being equal to or higher than PIQ scores in both left and right hemispherectomised patients than the converse situation. It is currently unclear as to whether this is a reflection of prioritisation of language skills (Mariotti 1998, Ogden 1989) or motoric difficulties/fatigue creating limitations as 4 of the 5 performance IQ subtests of the WISC, and 3 of the 5 performance IQ subtests of the WAIS are dependent on performing motor functions to solve a problem within a specified time limit. There are no concessions made for performing a task with only one hand, resulting in a potential negative bias for individuals with hemiplegia.

Although these verbal-performance IQ discrepancies are interesting, there are also studies that include hemispherectomised patients with no discrepancies between Verbal IQ and Performance

IQ, with a general reduction in intellectual function being the most prominent finding (Griffith 1967, Ignelzi 1968, Kohn 1974, Dennis and Whitaker 1976, Verity 1982, Vargha-Khadem 1991, Kalkanis 1996, Pulsifer 2004). With the exception of Pulsifer, many of these studies employed single case studies, or comparison of between 2 and 10 hemispherectomy cases resulting in difficulties obtaining a general overview of IQ data in hemispherectomy studies. It is most likely that all these observations are insightful fragments of the broad spectrum of possible neurocognitive outcomes in this patient group. The study described within this thesis employed a relatively large patient group (n = 22) in order to obtain a more general overview of IQ measures, and to make comparisons according to side of hemispheric removal and one versus two functional hemispheres.

It is also important to mention the deleterious effects of seizure disorders on IQ measures. Studies comparing children with unilateral cerebral lesions have noted differences in IQ scores according to whether seizures are present (Vargha-Khadem 2000). Reviews of neuropsychological profiles in childhood epilepsy (Milner 1975, Lassonde 2000, Elger et al 2004), illustrates both general and specific impairments according to the location of the epileptogenic focus. Neville (1999) also confirms the broad spectrum of behavioural, cognitive and motor outcome as a result of seizure activity. Due to the heterogeneity within the control group with regards to seizure foci, specific effects on verbal and performance IQ were not expected for the group measures.

2.2.2 Aims and predictions

The principal aims of measuring general intellectual functions were (1) to establish baseline measures of general intellectual function in patients and controls; (2) to determine whether the matching process between patients and controls was successful; (3) to determine the relationship between side of hemispheric injury and verbal/performance IQ scores; (4) to address the effect of age at seizure onset and seizure duration on task performance.

Between groups comparisons of neuropsychological data from the patient and control groups were carried out. The predictions were as follows:

- A trend towards higher verbal than performance IQ scores in both left and right hemispherectomy groups is expected based on previous findings and the concept of prioritisation of verbal functions in the isolated hemisphere.
- A relationship between age at onset of seizures and performance IQ scores is expected in left hemispherectomised patients, based on the possibility of early lesions disrupting the development of non-verbal skills.

2.2.3 Methods

2.2.3.1 General overview

The Wechsler Intelligence Scale for Children (WISC-III) (Wechsler 1992) was administered to participants up to the age of 16:11, and the Wechsler Adult Intelligence Scale (WAIS-III) (Wechsler 1997) was administered to participants aged 17 years or above. These tests of intelligence consist of several subtests that are broadly split into a verbal and a non verbal (performance) scale. The verbal subtests are designed to assess an individual's ability for verbal expression, understanding of verbal concepts and abstract reasoning. The performance subtests assess visual and spatial organization and perceptual ability.

2.2.3.2 *Description of subtests – verbal scale*

<u>Information:</u> a series of orally presented questions measuring an individual's knowledge of common events, objects, places, and people.
<u>Similarities:</u> a series of orally presented word pairs, for which an individual has to explain the similarity between the objects or the concepts, which they represent.
<u>Arithmetic:</u> a series of arithmetic problems, which an individual solves mentally and responds to orally.
<u>Comprehension:</u> a series of orally presented questions that requires an individual to solve everyday problems or to show understanding of social rules or concepts.
<u>Digit Span:</u> a series of orally presented number sequences which an individual has to repeat verbatim, and subsequently has to repeat a sequence of numbers in their reverse order.
<u>Vocabulary:</u> a series of words presented orally which an individual has to define.

2.2.3.3 Description of subtests - Performance Scale

<u>Picture Completion:</u> a set of pictures of common objects and scenes that all have an important part missing which an individual has to identify.
<u>Digit Symbol - Coding:</u> a series of single digit numbers each paired with a simple symbol provides a key. An individual uses the key to draw missing symbols under a series of digit numbers within a time limit.
<u>Picture Arrangement:</u> a series of pictures describing a story but presented in the wrong order. An individual has to understand the causal relationships in the story and place the pictures in the right order within a specified time limit.
<u>Block Design:</u> an individual is given three-dimensional blocks composed of two colours which are used to reproduce a two dimensional abstract pattern within a specified time limit.

Matrix Reasoning (WAIS-III only) - an individual looks at a matrix from which a section in missing and has to identify out of five response options, which completes the matrix. The task consists of four types of reasoning, pattern completion, classification, analogy, and serial reasoning.

Object Assembly (WISC-III only): a set of jigsaw puzzles of common objects, which the individual assembles to form a meaningful whole within a specified time limit.

All the subtests from the verbal and performance scales were administered. Scaled scores (raw scored adjusted for chronological age) were calculated for each subtest according to instructions specified in the relevant test manual. Verbal and Performance IQ's were then calculated from scaled scores, again using instructions specified in the relevant test manual. Subtest scaled scores have a mean of 10 and a standard deviation of 3 (average range 7-13), and IQ scores have a mean of 100 and a standard deviation of 15 (average range 85-115). Percentile scores reflect the percentage of the population that would obtain lower or equivalent scaled scores.

2.2.4 Data analysis

Statistical analysis of neuropsychological data that were related to specific a priori predictions were carried out using comparison of means tests. Where examination of the data did not rest upon specific a priori predictions, statistical analyses of neuropsychological data were carried out using analyses of variance (ANOVA) to examine possible interactions of between subject factors. Two way ANOVAs were carried out with two between subject factors of hemisphere (left vs right hemispheric removal) and group (hemispherectomised patients vs controls) to assess for significant differences on the dependent variables relating to neuropsychological measures. Effects of side of hemispheric removal could only be interpreted from the interaction between presence or absence of surgery and side of hemispheric removal, since the main effect of side of hemispheric removal would be averaged across patient and control groups (left = left hemispherectomised patients and controls, right = right hemispherectomised patients and controls) The presence or absence of an interaction between surgery and side of hemispheric removal was considered first. If significant, this was interpreted using comparison of means tests. If the interaction was not significant, the presence or absence of a main affect of group and/or side on the dependent variables was considered and interpreted.

Where assessments included more than one condition, mixed model analyses were used, with presence or absence of surgery (group) and side of hemispheric removal (hemisphere) as between subjects factors, and the assessment condition as within subjects factor. The F ratios and p values were obtained using Greenhouse-Geisser degrees of freedom adjustment of within subjects effects. This adjusts for correlation among the observations, and is necessary since the within subject measures were not expected to satisfy the independent errors assumption that underlies the conventional ANOVA calculation. The adjustment is negligible if the observations are effectively independent. In cases where within subject factors had only two levels, Greenhouse-Geisser adjustments are unnecessary, as correlation between resulting pairs of observations does not affect the validity of the conventional F test, as sphericity holds by definition. Significant within subject main effects were analysed post hoc by t tests using Bonferroni correction where appropriate.

The homogeneity of variance of the ANOVA model was checked using Levene's test on the residuals of the model. Where the assumption of normally distributed residuals and homogeneity were violated, non parametric statistics were used, e.g. the Mann-Whitney U test. This was not always possible, since standard non parametric tests do not permit covariate adjustment. In cases where covarying was required, but data were not normally distributed, or variances were not equal, parametric tests were used since the effects of related variables were considered to be important in the interpretation of the results. In these cases, violations are stated and results are interpreted with caution.

The predictive significance of factors such as age at onset of seizures and duration of seizure disorder prior to surgery on task performance was determined using simultaneous multiple regression or correlational analyses. A large number of statistical tests were performed for these studies, and therefore, the overall probability of a type 1 error is expected to exceed 5 percent. A formal multiple comparisons adjustment would reduce the power of detecting expected group differences e.g., those relating to the effects of surgery, side of injury or age at injury. However, a specific pattern of results across a range of tasks including both intact and impaired performance was predicted for this thesis. A formal correction for multiple comparisons was therefore made only when interpretation of an interaction involved more than two levels of comparison. Findings were interpreted using an approach that utilised Fisherian principles (Efron and Gous 2001) using these guidelines: p-values of 0.01- 0.05 were taken as evidence of an effect, while p-values of 0.001 were taken as strong evidence of an effect. Furthermore, only the results of significant tests that were associated with strong prior probability were given a strong interpretation. Any results of significant tests that had not previously been predicted were interpreted with caution, and taken as indicators for future studies with a similar group of patients.

2.2.5 Results

2.2.5.1 Descriptive statistics and ANOVA results for IQ measures

Figure 2.1 shows the results of the verbal and performance IQ scores for the patient groups only. Table 2.14 shows the results of the verbal and performance IQ assessment for the patient and control groups, as illustrated by figures 2.2 and 2.3. Discrepancies in Verbal and Performance IQ were examined using repeated measures ANOVA. Between subjects factors of group (hemispherectomy vs control) and hemisphere (left vs right) were used, with Verbal and Performance IQ as within subject factors. There were no effects, which suggests similar Verbal and Performance IQ scores in each group. A closer look at individual scores however, illustrates some discrepancies in scores.

Table 2.14. IQ standard scores (mean +/- SEM).

Subject group	VIQ	Range	PIQ	Range
Left hemispherectomy	71.8 (3.3)	52 - 95	65.5 (3.7)	49 - 89
Left controls	74.6 (5.8)	46 - 103	70.3 (3.8)	53 - 90
Right hemispherectomy	71.7 (5.5)	48 - 95	63.7 (4.2)	46 - 91
Right controls	68.6 (4.6)	50 - 93	71 (4.8)	56 - 99

Figure 2:1. IQ standard scores - hemispherectomised patients (mean +/- SEM)

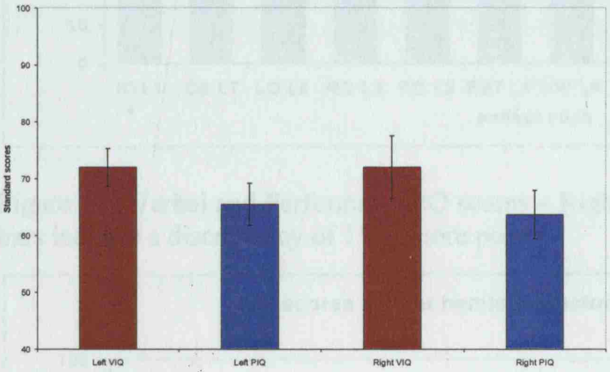


Figure 2:2. Verbal IQ standard scores (mean +/- SEM)

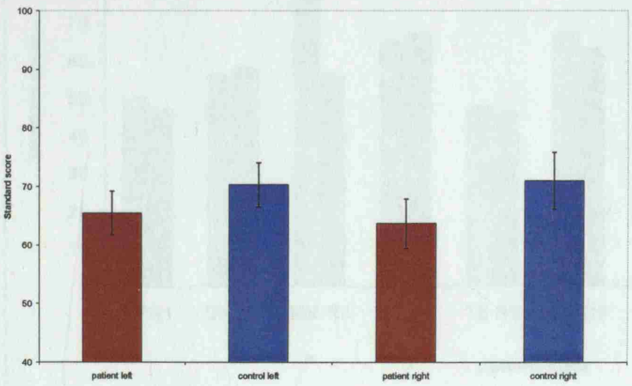


Figure 2:3. Performance IQ standard scores (mean +/- SEM)

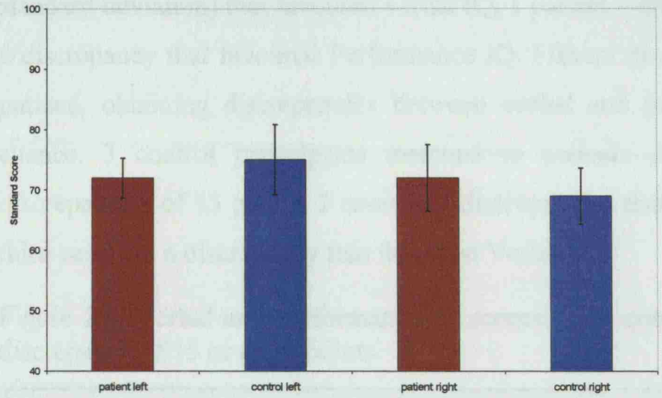


Figure 2:4. Verbal and Performance IQ scores – Left hemispherectomised patients. Asterisked cases indicate a discrepancy of 15 or more points

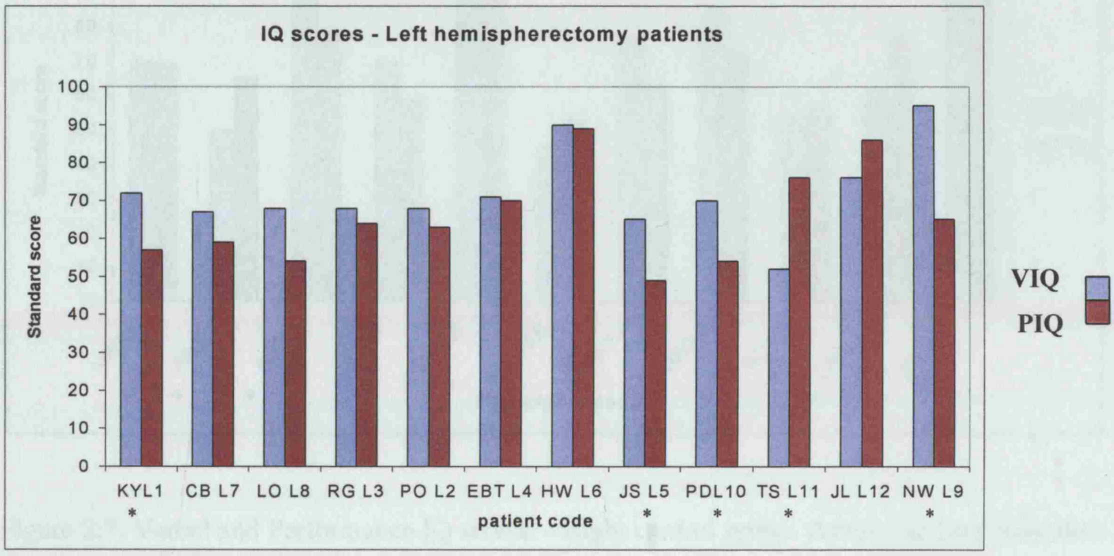
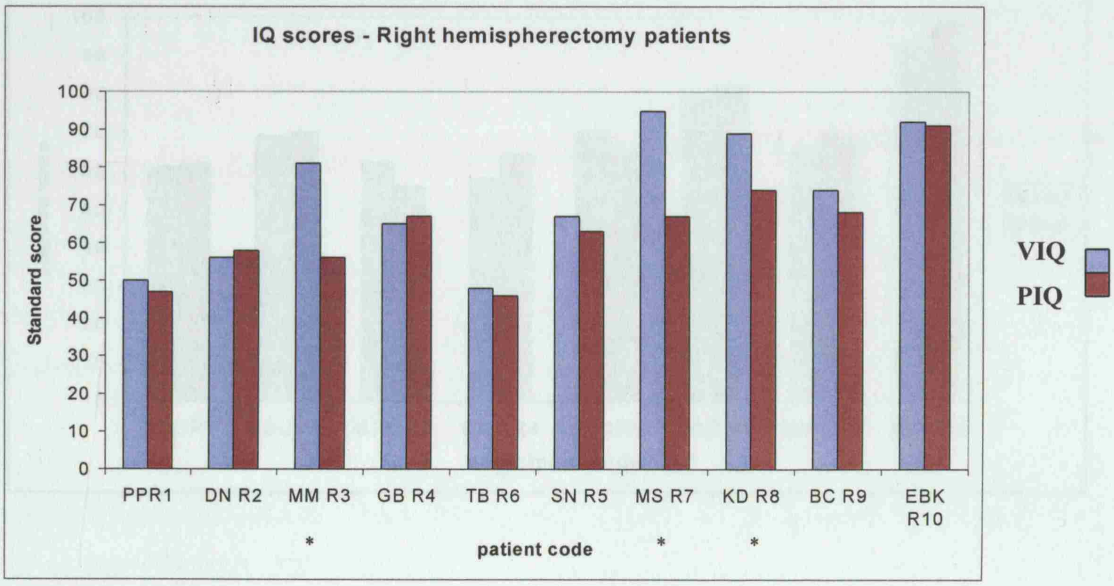


Figure 2:5. Verbal and Performance IQ scores – Right hemispherectomised patients. Asterisked bars indicate a discrepancy of 15 or more points.



Eight hemispherectomised patients (5 left, 3 right) had a discrepancy of 15 or more points (1 standard deviation) that favoured verbal IQ, 1 patient with onset of left sided pathology at 6 had a discrepancy that favoured Performance IQ. Fishers exact test revealed that the proportion of patients obtaining discrepancies between verbal and performance IQ was not greater than chance. 3 control participants matched to patients with left hemispherectomy also had discrepancies of 15 points, 2 cases had discrepancies that favoured Performance IQ, whilst the third case had a discrepancy that favoured Verbal IQ.

Figure 2:6. Verbal and Performance IQ scores – left control group. Asterisked bars indicate a discrepancy of 15 or more points.

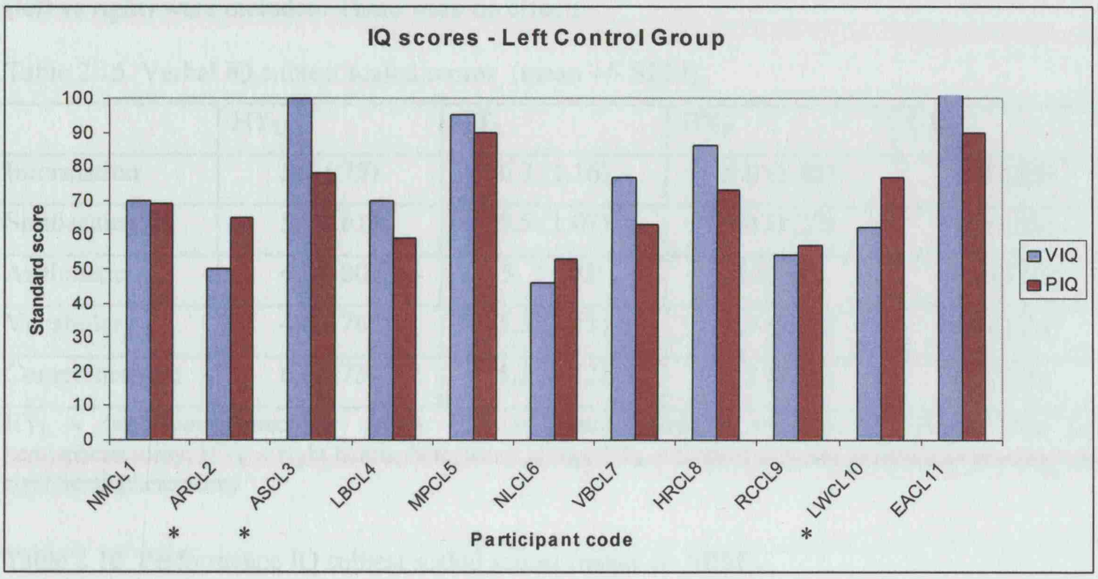
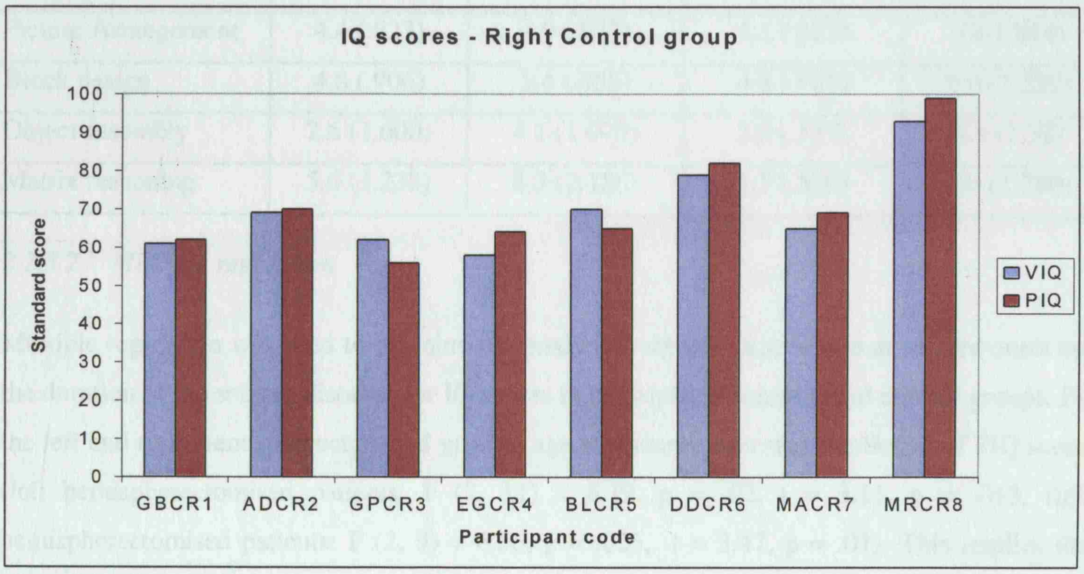


Figure 2:7. Verbal and Performance IQ scores – Right control group. Asterisked bars indicate a discrepancy of 15 or more points.



Repeated measures ANOVA using the within subjects factors "subtest-viq" was carried out to examine possible strengths and weaknesses in each group for the verbal IQ subtests. Between subjects factors of group (hemispherectomy vs control) and hemisphere (left vs right) were included. Statistical analysis showed no evidence for an interaction between hemisphere and group. There was a main effect of subtest (ANOVA: $F(1, 37) = 3.023$, $p = 0.025$). Repeated measures ANOVA using the within subjects factors "subtest-piq" was carried out to examine possible strengths and weaknesses in each group for the performance IQ subtests. Matrix reasoning and object assembly were excluded as they are not regular subtests of both the WISC and WAIS. Between subjects factors of group (hemispherectomy vs control) and hemisphere (left vs right) were included. There were no effects.

Table 2.15. Verbal IQ subtest scaled scores (mean +/- SEM).

	HY_L	CT_L	HY_R	CT_R
Information	5.7 (.75)	6.3 (1.16)	5.0 (1.15)	4.9 (.85)
Similarities	5.7 (.61)	5.5 (1.07)	5.4 (1.27)	4.8 (.98)
Arithmetic	4.0 (.80)	5. 2 (.93)	4.0 (65)	4.4 (1.07)
Vocabulary	4.6 (.76)	5.2 (1.11)	5.5 (1.35)	4.5 (1.24)
Comprehension	6.0 (.73)	5.3 (1.12)	6.2 (1.04)	5 (1.18)

HY_L = left hemispherectomy group; CT_L = control subjects matched to patients with left hemispherectomy; HY_R = right hemispherectomy group; CT_R = control subjects matched to patients with right hemispherectomy

Table 2.16. Performance IQ subtest scaled scores (mean +/- SEM).

	HY_L	CT_L	HY_R	CT_R
Picture Completion	4.7 (.689)	4.8 (.749)	4.5 (1.176)	6.0 (.707)
Coding	4.0 (.389)	6.3 (.864)	2.8 (.554)	4.8 (1.013)
Picture Arrangement	4.4 (.823)	4.9 (.977)	4.1 (.623)	4.6 (.844)
Block design	4.8 (.906)	5.4 (.856)	4.8 (.987)	6.0 (1.239)
Object assembly	2.6 (1.600)	4.1 (1.079)	2.0 (.557)	4.5 (1.32)
Matrix reasoning	5.6 (1.232)	8.3 (2.186)	5.7 (.558)	7.0 (1.780)

2.2.5.2 Multiple regression

Multiple regression was used to examine the predictive significance of age at seizure onset and the duration of the seizure disorder for IQ scores in hemispherectomised and control groups. For the left and right hemispherectomised groups, age at seizure onset was predictive of PIQ scores (left hemispherectomised patients: $F(2, 11) = 6.19$, $p = .02$, $t = 3.11$, $p = .013$, right hemispherectomised patients: $F(2, 9) = 6.56$, $p = .025$, $t = 3.47$, $p = .01$). This implies that hemispherectomised patients with earlier onset of seizures tend to obtain lower performance IQ scores. There were no other significant results.

2.2.6 Discussion

2.2.6.1 General level of intellectual function after hemispherectomy

In summary, mean IQ scores for hemispherectomised patients were severely impaired, a finding that is generally consistent with the literature (Wyllie 1998, Devlin 2003, Pulsifer 2004). Although there are case reports of hemispherectomised patients obtaining IQ scores within the average range (Damasio 1975, Sergent and Villemure 1989, Vanlancker 2004), they are few and far between. In this study, left hemispherectomised patient **HW $_{L}$6** obtained VIQ and PIQ scores of 90 and 89 respectively, and right hemispherectomised patient **EBK $_{R}$10** obtained VIQ and PIQ scores of 92 and 91 respectively. Three patients (**NW $_{L}$9, KD $_{R}$8, MS $_{R}$7**) obtained a VIQ score within the average range, and left hemispherectomised patient **JL $_{L}$12** obtained a PIQ score within the average range. There are no obvious common factors shared by these patients despite suggestions from previous research relating favourable cognitive outcome in hemispherectomised patients to duration of seizure disorder (Villemure and Rasmussen 1993), pre operative cognitive function (Maehara 2002, Rasmussen 1989), age at surgery (Humbertclaude 1997) and type of pathology (Doring 1999, Pulsifer 2004). Although these cases represent a minority, they confirm previous reports that the isolated left or right hemisphere can maintain age appropriate levels of general verbal and non verbal reasoning ability. This in turn, raises questions regarding why so many hemispherectomised patients achieve below average IQ scores despite being seizure free. Impaired intellectual function in these patients may reflect the possibility of secondary generalization of seizures to the intact hemisphere resulting in the development of aberrant connectivity (Gall 2004, Jahan 1997, Swann 2004, Blume 2004) or persistent subclinical epileptiform activity (Doring 1999) thus precluding optimal functioning of the isolated hemisphere. Residual damage to the intact hemisphere is an attractive suggestion, though the exact nature of impairment and its relationship to cognitive impairment remains to be elucidated by electrophysiological, neuroimaging and post mortem studies.

2.2.6.2 Comparison of patients and controls

There were no significant differences between hemispherectomised patients and control participants relating to age and IQ measures, suggesting the groups were reasonably well matched. This will facilitate further comparisons throughout the thesis as variables such as age, gender and IQ are accounted for, thus enabling analysis of the relationship between general level of cognitive function and performance on visual cognitive tasks without the confounding effects of these variables.

2.2.6.3 Comparison according to side of hemispheric removal

Comparisons for side of hemispheric removal revealed no differences in verbal and performance IQ measures and their related subtests. These results are consistent with previous studies, as they refute theories of early specialisation and are taken as support for the equipotentiality hypothesis discussed in chapter one. There are several points to be considered before one can conclude that the isolated left and right cerebral hemispheres are equally capable of subserving verbal and non-verbal functions. Firstly, the possibility of group means masking discrepancies in small heterogeneous groups must be acknowledged. It may also be the case that the relationship between IQ measures and hemispheric function is over estimated, particularly the relationship between PIQ scores and right hemisphere function. The Wechsler scales have been criticized previously for failing to provide an accurate assessment of right hemisphere functions (Ogden 1989, Lezak 1988). Another shortfall in IQ measurements is that cognitive strengths and weaknesses are buried within a single index, and it becomes incredibly difficult to ascertain the nature or the severity of impairment in different cognitive domains, even when considering subtest scores. Although IQ scores provide a useful baseline measure of intellectual function, a more detailed battery of neuropsychological tests that are specific to the functions being investigated is needed to reveal any subtle differences in the capacity of the isolated left and right hemispheres (Day and Ulatowska 1979, Ogden 1989).

2.2.6.4 VIQ-PIQ discrepancies

There were no significant VIQ-PIQ discrepancies for any of the groups. These results accord with the literature, and appear to contradict the crowding hypothesis, which predicts higher verbal than non-verbal cognitive capacity due to prioritising language in the face of limited processing space. Again there are important points to consider before concluding that there is no evidence of crowding in the hemispherectomised group. The possibility of group means masking discrepancies in small heterogeneous groups must always be addressed. When adopting a similar approach to previous studies by taking a closer look at single cases, it became evident that some patients had Verbal and Performance IQ discrepancies that were separated by 1 standard deviation or more, and almost always in favour of Verbal IQ, regardless of side of pathology. It becomes clear why studies using single cases or extremely small numbers appear to present conflicting results. It seems there exists a range of outcomes after hemispherectomy with regards to Verbal and Performance IQ measures, and though the majority of patients (64%) do not have a large discrepancy in scores, the tendency of 32% of this study group to have lower performance IQ must be acknowledged.

It is of some interest that of the left hemispherectomised patients who showed a discrepancy between verbal and performance scores, all but one case was in favour of verbal IQ. Two cases (**KY_L1**, **JS $_L$5**) had congenital injuries, which suggest the right hemisphere may have always mediated linguistic functions in these patients. Previous studies show an increase in right hemisphere dominance for language following early left hemisphere injury (Rasmussen and Milner 1977, Woods 1988, Chilosi et al 2005). Case **KY_L1** suffered intractable seizures from 4 months of age, providing an early impetus for right hemisphere language development. Seizure onset in case **JS $_L$5** was considerably later at 3 years of age, though language appeared to be unaffected by the seizure disorder, suggesting right hemisphere mediation. The apparent failure of the right hemisphere to mediate visuospatial functions related to performance IQ tasks may relate to previous suggestions about competition for neural processing space, and the prioritisation of linguistic capacity as opposed to functions classically ascribed to the right hemisphere (Teuber 1974, Ogden 1988, Marriotti 1998).

The other two left hemispherectomised patients with higher Verbal than Performance IQ scores acquired injuries after the first year of life, raising the possibility of reorganisation of function. It is of note that both of these cases were originally right handed, and subsequently changed preference during the course of the disease prior to surgery. An early unilateral lesion that modifies hand preference will often change speech representation (Rasmussen and Milner 1977), though it is acknowledged that motor dominance can shift independently of language (Rey 1988) and vice versa (Satz 1988). Case **NW $_L$9,** had a cerebrovascular incident at 18 months of age that resulted in a right hemiplegia, forcing shift of hand preference. Seizures began 2 years later, with evidence of global intellectual impairment, though speech arrest was not evident. Seven years post operatively, the verbal IQ was within the average range, yet the performance IQ was severely impaired. Case **PD_L10,** developed Rasmussen's Encephalitis in the left hemisphere at 3:7. He was originally right handed, and speech regression was noted during the acute phase of the disease. Remarkably, his hand preference switched within 8 weeks of disease onset at which point speech also dramatically improved. Nine years post operatively, the Verbal IQ was in the borderline range, but Performance IQ was severely impaired.

There is an interesting comparison between the aforementioned left hemispherectomised patients and case **TS $_L$11**, whose seizure disorder began at six years of age as a result of Rasmussen's encephalitis. This patient was also previously right handed and switched preference during the course of the seizure disorder, but in contrast to cases **NW $_L$9** and **PD_L10**, she is the only patient to show a discrepancy between Verbal and Performance IQ greater than one standard deviation in favour of the latter. Speech regression was noted during the course of the disease as with **PD_L10**, but recovery of linguistic function was not observed prior to surgery and subsequent progress over the last 6 years has been slow with respect to speech production. This implies that that reorganisation and development of language functions in the right hemisphere at this age may be somewhat limited, perhaps due to limitation of available substrate as a result of prior establishment of visuospatial skills (Marriotti 1998). Incomplete transfer of language function during the course of the seizure disorder may have resulted in bilateral dependent language representation, which is known to increase in prevalence after left hemisphere injury (Liegeois 2004, Loring 1999). Subsequent removal of the left hemisphere would thus result in language difficulties, as the left hemisphere was still partially responsible for linguistic function.

The idea of bilateral language representation prior to surgery resulting in subsequent linguistic deficits is also supported by data from case **JL $_L$12**, the only other case that has marked word-finding difficulties, yet his performance IQ is within the average range. This case is of particular interest as the only left hemispherectomised patient in this series with acquired disease that has always been left handed. Case **JL $_L$12** developed Rasmussen's encephalitis at 10 years of age. He became dysphasic during the course of the disease, suggesting left hemisphere language involvement. Remarkably at 8 years post surgery his Verbal IQ score is considerably higher than case **TS $_L$11** and the discrepancy between Verbal and Performance IQ scores, whilst in favour of Performance IQ is slightly smaller. It is possible that the right hemisphere was involved with linguistic function prior to disease onset, as 15 % of left handed individuals are known to have bilateral representation of language function (Rasmussen and Milner 1977). Whilst this may have afforded some preservation of linguistic function in the context of left hemisphere disease acquired in late childhood, lack of available substrate for complete transfer to the right hemisphere due to prior establishment of visuo-spatial skills may have contributed to persistent word finding difficulties.

Collectively, data from these isolated cases suggest that as development proceeds, there may be some limitations in reorganisation of language in the isolated right hemisphere, as visuospatial skills appear to become more impervious to the effects of left hemisphere damage. When brain injury occurs earlier, development of lateralised function becomes sidelined, and language appears to be mediated in the right hemisphere at the expense of maturation of visuospatial skills in some patients. These suggestions are supported by the results of the multiple regression analyses, which raise the possibility of performance IQ scores being higher in patients whose seizures begin later in childhood. Of course this is not a straightforward story of combat between verbal and visuospatial skills, as there is no corresponding relationship between age at seizure onset and verbal IQ scores in these patients. It seems that language will develop to some degree in most patients regardless of age at seizure onset, but the integrity of visuospatial skills in the right hemisphere could be more sensitive to this variable.

Three right hemispherectomy cases had a verbal – Performance IQ discrepancy in favour of the former. There does not appear to be a relationship to age at injury with respect to these cases, as case **MM $_R$3** had congenital injury, and cases **MS $_R$7** and **KD $_R$8** acquired Rasmussen's encephalitis at 4:6 and 5:0 respectively. These findings accord with previous studies reporting IQ measures in hemispherectomised patients (Ignelzi and Bucy 1968, Dennis and Kohn 1975, Ogden 1989). The discrepancy in favour of VIQ is less surprising in these cases as the left hemisphere remains in situ. It is of note that despite the apparent heterogeneity of possible outcomes after hemispherectomy, there are no reports of right hemispherectomised patients that have a VIQ-PIQ discrepancy in favour of the latter, and the results from the current study are consistent with this. Collectively, results from individual cases imply that verbal intelligence will be prioritised regardless of side of hemispheric removal, with the exception of late left hemisphere damage. The timing of such damage may preclude complete transfer of language function to the right hemisphere, regardless of whether shifts in motor dominance occur.

Although data from these cases provide insight into possible reasons for discrepancies in Verbal and Performance IQ scores, it must be acknowledged that 64% of cases have no discrepancy. Two cases have scores close to floor level, hence there is no opportunity to observe discrepancies. Of the remaining 14 cases, 10 had no more than 5 point difference between verbal and performance IQ scores, 3 cases had differences between 6-14 points in favour of Verbal IQ (**CB $_L$7, LO $_L$8, BC $_R$9**), and one patient had a difference of 10 points in favour of Performance IQ (**JL $_L$12**). It may be the case that the isolated hemisphere tends towards similar levels of verbal and non verbal function, though it is also possible that differences become less evident when scores are in the severely impaired range, a point raised previously by Smith and Sugar (1975). Although a VIQ-PIQ discrepancy within 15 points is deemed to be insignificant in the normal population, it is possible that smaller differences may be significant for individuals with brain injury and cognitive limitations (Kaufman 1994). The Wechsler scales have also been criticized for the amount of overlap between cognitive resources needed for VIQ and PIQ subtests, thus reducing the possibility of observing differences in verbal and non-verbal intelligence. The presence of cognitive impairment and limitations in the Wechsler scales with regards to partitioning cognitive resources for different subtests may be additive in reducing the amount of differences observed in patients with cognitive impairments.

It is doubtful that a single explanation can account for the range of IQ outcomes observed after hemispherectomy. Whilst cognitive impairment and limitations of the Wechsler scales may account for lack of VIQ-PIQ discrepancies found in some cases, there are also instances in which the isolated hemisphere subserves both verbal and non verbal intelligence to a similar level within the average range, thus supporting the possibility of hemispheric equipotentiality. Left hemispherectomised patient **HW $_L$6** and right hemispherectomised patient EBK $_R$**10 are** examples of such cases.

2.2.6.5 Relationship between age at onset of seizures and PIQ scores

Multiple regression analyses suggest that hemispherectomised patients with early onset of seizures tend towards lower Performance IQ scores. This finding is unsurprising in left hemispherectomy cases if one considers the relationship between advancing age and ability to reorganize linguistic function. It is possible the right hemisphere become increasingly resistant to crowding as development proceeds. The suggestion that right hemispherectomised patients with relatively late onset of seizures would have better performance IQ scores than patients with early onset right hemisphere injuries may seem unusual. There are several possibilities for these results. As mentioned in previous sections (1.4 and 2.2.1), early right hemisphere damage seems to be particularly deleterious to cognitive development. Another possibility is that visuospatial functions become bilaterally represented to some degree as development proceeds (Sergent and Villemure 1989). If the integrity of the right hemisphere is instrumental in the establishment of such representations, it follows that early as opposed to later damage would result in poor representation of non-verbal functions in the left hemisphere. It may also be the case that the relationship between performance IQ and right hemisphere function is over estimated as mentioned earlier, such that no clear relationship exists between Performance IQ scores and integrity of right hemisphere function. The relationship between age at onset of seizures and visuospatial function will be addressed in more detail in subsequent chapters.

2.2.6.6 Summary

In general, the results reported in this study population are concordant with the literature documenting impaired levels of general cognitive function in hemispherectomised patients. There were no side specific differences in VIQ and PIQ measures, and a general lack of discrepancy in Verbal and Performance IQ scores. Although some patients did have a discrepancy between verbal and performance IQ, the proportion obtaining such discrepancies was not statistically significant. Use of small, heterogeneous groups warranted a closer look at individual cases, to determine whether results obtained accord with previous suggestions of hemispheric crowding, and the interaction between age at injury and degree of hemispheric lateralisation of function. Several cases obtained scores that were compatible with the concept of crowding, and VIQ-PIQ differences in favour of the former lend support to the assertion that the two hemispheres have at least some degree of equipotency with respect to language. VIQ-

PIQ differences in the opposite direction highlight the importance of the timing of left hemisphere injury and the development of verbal intelligence. Patients with Performance IQ scores approaching the average range are of particular interest in this study. Subtle impairments in visuospatial processing have been previously reported in hemispherectomy cases in the context of intact performance IQ scores (Sergent and Villemure 1989). Whilst the Wechsler scales provide a baseline measure of verbal and non verbal function in these patients, and discrepancies were interesting, a more detailed battery of tests are needed to examine the various domains of visuospatial processing, including tests that do not depend on timed motor performance. As mentioned in chapter one, previous literature is extremely sparse, with only a small number of studies presenting results of visuospatial tests, and in only three of these reports (Kohn and Dennis 1974, Ogden 1989, Sergent and Villemure 1989) were visual cognitive functions the principal focus of the investigation. The following chapters present results from a detailed battery of visuospatial tests administered to hemispherectomy and control groups, in an attempt to build upon previous studies and to chart new territory with respect to the detailed investigation of non-verbal functions in these patients.

3 Stereopsis after hemispherectomy

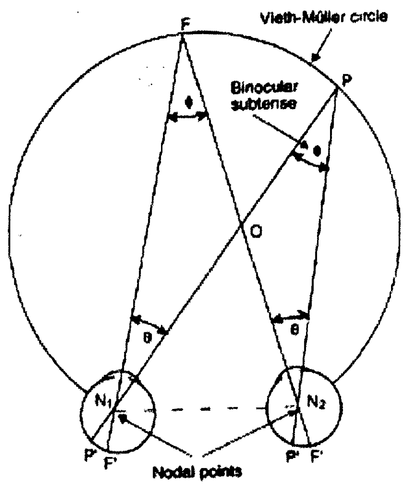
3.1 Introduction

This chapter reports the results of stereopsis testing in hemispherectomised patients. After defining the mechanisms contributing to stereoscopic vision and relevant anatomy to determine whether stereopsis is likely to be present in these patients, the developmental trajectory of acute stereopsis is outlined to illustrate its protracted course of maturation. This is important when considering the possibility of a relationship between age at brain injury and levels of stereoacuity. Results are then reported and discussed in relation to factors that may obstruct or facilitate performance on tests of stereoscopic vision in this patient group.

3.1.1 The anatomy of stereopsis

Stereoscopic vision, the perception of depth based on retinal disparity cues, is a product of interpupillary distance creating slight differences in retinal images at any given point outside the plane of zero disparity – the horopter (see fig 3.1). The theoretical horizontal horopter is circular (Vieth 1818, Muller 1926), lying within the visual plane and passing through the fixation point F and nodal points (N1 and N2) of the two eyes (Figure 3.1). Any point on the circle can be imaged at equal retinal eccentricities in the two eyes. The horopter thus represents zero disparity. Any points that do not lie on the circle or the midline horopter (vertical line extending north and south of the fixation point), project to the retina with vertical and /or vertical and horizontal disparity. The image falls on disparate retinal loci in each eye, signalling a shift either towards or away from the horopter thus signalling depth relative to the fixation point.

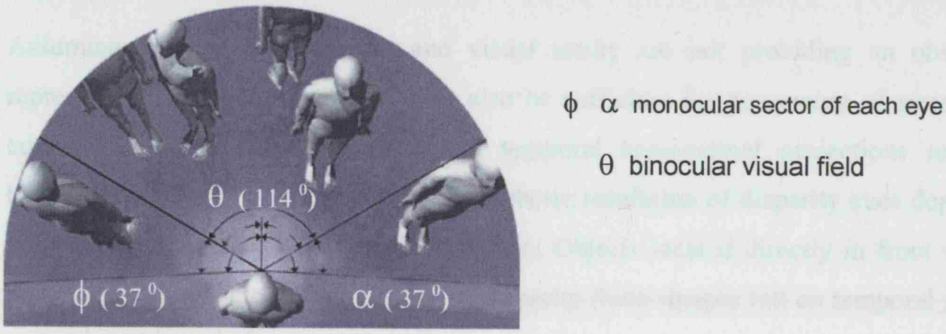
Figure 3:1. The theoretical horopter and fusion areas (Howard 2002)



When the eyes converge on point F, foveal images F' have zero disparity. A circle drawn though point F and the nodal point of each eye represents the horizontal horopter (Vieth-Muller circle). Any point P on the circle has a binocular subtense of ϕ, as all points project from N1 and N2 to the horopter. As the opposite angles at O are equal, so are angles Θ. Any points along the circle thus represent zero disparity, as their angles remain constant and thus images fall on corresponding points in each retina.

The binocular visual field is the portion of the total visual field within which an object is visible to both eyes for a given fixation point (see figure 3.2). The field extends approximately 114 degrees when the eyes converge symmetrically, with upper and lower boundaries of 50 and 75 degrees respectively. Binocularly corresponding points, when stimulated separately, are associated with the same visual direction. If the images falling on corresponding retinal points are similar, they fuse into a single percept. Binocular disparity for certain components of the image forms the basis of stereoscopic depth perception, as stimuli do not need to fall on exactly corresponding retinal points to create a single percept. Each retinal point in one eye is associated with a small area in the other eye (Panums fusional area), thus any pair of similar stimuli that fall within this area are perceived as a single object. Disparity between the positions of the two stimuli creates depth perception relative to the point of fixation.

Figure 3:2. Divisions of the visual field with respect to binocular vision



The amount of disparity is related to the magnitude of perceived depth relative to the fixation plane. Thus, points on a 3-D object just outside the fixation plane will stimulate different points on each eye, providing multiple cues from which to derive 3-D structure. There are two prerequisites to fusion of binocular input at this stage, namely visual acuity and alignment of the visual axes of each eye. Visual acuity of each eye must be sufficient to produce input that is similar in resolution, thus permitting fusion. An important cause of acuity related monocular suppression is a difference in refractive errors of the two eyes termed anisometropia (Tomac 2001). Information from the weaker eye is suppressed, depriving the visual cortex of binocular input and preventing stereopsis. Anisometropia may thus account for impaired stereopsis in children with apparently normal binocular visual acuity (Tomac 2001).

Alignment of the visual axes is also crucial for stereopsis. Binocular input must be derived from Panum's area, requiring optimal oculomotor co-operation between the eyes when fixating. Strabismus of sufficient magnitude will therefore result in diplopia and subsequent monocular suppression, thus precluding stereopsis (Dobson 1989, Keenan and Willshaw 1992). Ocular alignment is an important issue in this thesis as unilateral exotropia of the eye ipsilateral to the lesion is an established method of visual field compensation in hemianopic patients (Herzau

1988, Levy 1995, Gamio 2003). The resulting deviation results in difficulty converging the visual axes on an intended object. In such cases of unilateral strabismus, one eye is consistently used for fixation with some degree of alternation between the two eyes. This prevents diplopia due to images of the same object falling on non-corresponding points on the two retinae. As a result, the image from the non-fixating eye is totally suppressed, depriving the visual cortex of binocular input and ultimately preventing stereopsis. Less severe forms of ocular misalignment may also account for absence or relatively coarse levels of stereopsis in patients without obvious strabismus. Microtropia results from small angle deviation of the visual axes and whilst stereopsis may still be present, it is often degraded as corresponding retinal images may reside in the outer limits of the fusional area (Rutstein and Eskridge 1984, Matsuo et al 2003). Further improvements are brought about by turning the head to refine ocular deviation within the limits of Panums area (Stager and Birch 1986).

Assuming that ocular alignment and visual acuity are not providing an obstacle, cortical representation of binocular input must also be sufficient for processing of stereoscopic depth cues. The arrangement of nasal and temporal hemi-retinal projections to the cerebral hemispheres affords both uni and bi hemispheric resolution of disparity cues depending on the position of the stimuli within the visual field. Objects located directly in front of the fixation point (see figure 3.3, p. 97) have crossed disparity (both images fall on temporal retinal points), and objects located directly behind the fixation point have uncrossed disparity (both images fall on nasal retinal points). This implies that interhemispheric co-operation is necessary for midline stereopsis, whereas images to the left or right of the fixation point will project to the corresponding cerebral hemisphere. Lehmann and Julesz (1978) found that when dynamic random dot stereograms (see appendix E) were confined to the left visual field, changes in perceived depth were followed by Visual Evoked Potentials (EVP) in the right hemisphere. The opposite was found for stereograms presented to the right visual field, with VEP's in the left hemisphere. Indeed, one important function of hemidecussation of optic nerves could be to bring inputs from a given part of the binocular visual field to the same location in the brain to enable comparison between roughly corresponding retinal points with a minimum length of connections (Howard 2002).

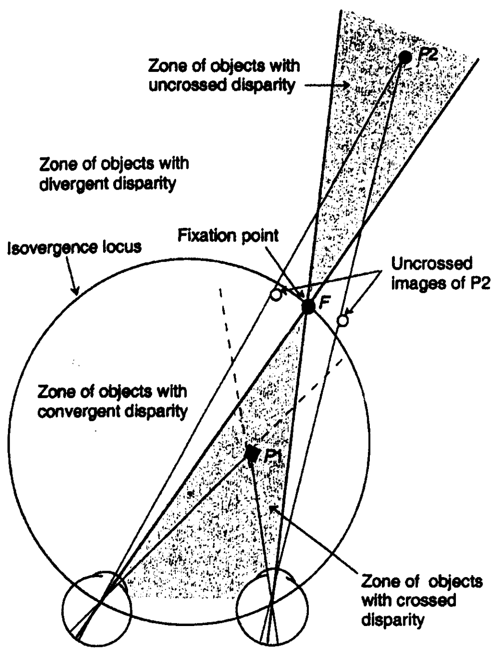
These findings imply that both hemispheres mediate stereopsis and co-operate to resolve centrally presented depth cues, which is at odds with claims that laterality effects exist in stereoscopic vision. Evidence for a functional laterality component in stereopsis is sparse and results are mixed. Manning (1992) and Skrandies (1997) found larger VEP responses when stimuli were presented to the right visual field, suggesting a left hemisphere advantage, whereas other studies demonstrated left visual field advantages upon viewing stereograms (Durnford and

Kimura 1971, Ptito 1993). fMRI studies have also demonstrated greater right hemisphere activation when viewing random dot stereograms (Kwee 1999, Fortin et al 2002, Nishida et al 2001). Studies of adults (Ptito et al 1988, 1991, Tsuda et al 1993) and children (Mercuri et al 1996) with unilateral cerebral injuries report deficits in stereopsis regardless of the side of the lesion, though Ptito and Tsuda comment that deficits are more common and more severe after right sided lesions. It is possible that hemisphere specific advantages and losses reported with stereoacuity tests are related to aspects of the task other than stereopsis such as form perception, reaction time, or use of extraneous cues. Differences between tasks and study populations prevent firm conclusions being drawn regarding the individual contributions of left and right hemispheres in resolving disparity cues, though it seems likely that it is a bihemispheric process. Further study is needed to confirm whether the isolated left and right hemispheres are capable of resolving binocular disparity cues, with the use of an appropriate control group as stereoacuity levels may be underestimated in individuals with cognitive impairment (Green 1977, Letourneau 1992).

A closer look at the neural substrates mediating stereopsis also lends support to the proposal that either hemisphere can resolve disparity cues. Neural substrates mediating stereopsis have been elucidated using single cell recordings and neuroimaging studies. Both magno and parvocellular systems are utilised in coarse and fine stereoscopic vision respectively, with primary registration of binocular input at the level of V1 (Schiller 1996). After monocular registration of input in ocular dominance columns, cortical neurones integrate inputs from both eyes, and binocular neurons respond to images that correlate. They are disparity selective, responding optimally to certain positional relationships between left and right eye images that provide the stimuli necessary for stereoscopic depth perception. It is also possible that some monocular neurones operate with a centre-surround system such that information from one eye is excitatory and the other inhibitory, thus disparity may be detected by variations in the balance between excitation and inhibition. Cells that respond to binocular disparity signals have been detected in striate and extrastriate cortex (Maunsell and Van Essen 1983, Poggio 1984). Primate studies reveal that V2 has a greater number of disparity selective cells than V1 (Poggio and Poggio 1984, Hubel and Livingstone 1987), and appears to be related to the detection of disparity defined edges. V3 has been linked to extraction of higher order disparities required for perception of 3D form (Paradis et al 2000). Disparity selective cells have been located in medial temporal and parietal components of the dorsal processing stream (Maunsell and Van Essen 1983, Taira 2000), and inferior temporal cortex of the ventral stream responds to shapes defined only by disparity cues (Tanaka 2001). PET studies of human visual cortex demonstrate bilateral activation when viewing random dot stereograms (Gulyas and Roland 1994). Activity was greatest along the calcarine sulcus, in the precuneus, the superior and lateral occipital gyri, with a similar areal extent in both hemispheres. The extrastriate cortex was most strongly activated, which accords with primate studies outlined previously. The involvement of these areas in stereoscopic vision is also supported by reports of loss of stereopsis in patients with extrastriate lesions.

Results from stereoacuity tests are rarely reported in studies documenting outcome after cerebral injuries. Early reports implicate bilateral posterior lesions in loss of stereopsis (Riddoch 1917, Holmes and Horrax 1919). More recent reports suggest that response to disparity cues may be compromised after unilateral occipital lesions, though reports remain sparse. Of interest are patients with contralateral homonymous hemianopia, as this field defect is observed in hemispherectomised patients. As there are no reports providing results of stereoacuity tests in hemispherectomised patients to date, these reports of patients with focal unilateral lesions offer useful if indirect insight into possible findings upon administration of stereoacuity tests to the patients in this current study group. The anatomical arrangement of stereopsis pathways suggest that disparity cues in the sagittal plane would be compromised in hemianopic patients, with sparing of stereopsis in more eccentric locations within the intact visual field.

Figure 3:3. Midline stereopsis and hemianopia (Howard 2002)



Note that objects P1 and P2 project bitemporally and binasally respectively; hence each hemisphere receives monocular input. Inter hemispheric co-operation is needed to compare corresponding retinal images for each eye to compute disparity.

If one hemisphere cannot process visual input, midline stereopsis is impossible unless uncrossed nasal or crossed temporal projections are present. Spared islands of vision may also contribute such that a portion of blind field is represented in the intact field. Simply turning the head and eyes to bring the objects away from the midline can also help.

A patient reported by Vaina (2002) had a right occipitotemporal injury that resulted in a left homonymous hemianopia without macular sparing. The patient lacked midline stereopsis as measured by random dot anaglyphs (see methods section 3.2.3). Hamsher also reports reduced stereoacuity after right hemisphere lesions (Hamsher 1978). Cowey (2000) reports a patient with left hemisphere damage causing right homonymous hemianopia with macular sparing. She was able to detect the presence of an area of depth when viewing random dot anaglyphs but was unable to identify the shape. The inability to identify the shapes was not the result of a generic impairment of shape processing, as she obtained scores within the average range when asked to identify shapes within an embedded figures task. Loss of midline stereopsis in hemianopes accords with anatomical observations which suggest that objects in the sagittal plane that fall in front of and beyond the horopter would project bi temporally and bi nasally respectively. Interhemispheric co-operation is hindered by blindness in the affected hemifield, thus depriving the intact hemisphere of binocular input.

There are however, reports documenting intact stereopsis in the presence of hemianopia. Hirai (2002) found that midline stereopsis was intact in all 9 hemianopic patients tested. Three possibilities that may help to explain presence of midline stereopsis in hemianopic patients are the degree of naso-temporal overlap of optic nerve fibres at the chiasma, the presence of macular sparing and subtle changes in head centred space during testing. It is possible that anomalous ganglion cell projections (uncrossed nasal and crossed temporal projections) create a narrow zone of naso-temporal overlap that is believed to exist in the region of the retinal vertical meridian (section 1.1). Wessinger (1996) carried out a study of visual field mapping of hemispherectomised patients and located a zone of spared vision along the vertical meridian up to 3^0 in diameter. He suggests that early cerebral insult may increase the likelihood of survival of anomalous projections, which opens up the possibility of a relationship between age at onset of pathology and probability of detecting islands of residual vision close to the vertical meridian. Although Wessinger did not investigate stereopsis, the finding of spared islands of vision in hemispherectomised patients with macular splitting may help to explain the presence of midline stereopsis in the context of hemianopia.

Evidence for an increase in the number of anomalous naso-temporal projections after early injury to the optic tracts comes from developmental studies of non-human primates (Bunt 1977, Leventhal 1988, Fukuda 1989). These studies have been criticized on methodological grounds as naso-temporal overlap can only be estimated and not actually visualized (Schein 1988) and estimates of 3^0 are deemed to be optimistic, with overlap of 0.5^0-1.5^0 being more realistic (Stone 1973, Wyatt 1978). Naso-temporal overlap would also suggest that the vertical meridian is represented bilaterally in visual cortex (Fendrich and Gazzaniga 1989), a suggestion that was not substantiated by imaging studies (Tootell 1988). Studies of patients with callosal agenesis (Jeeves 1991) and callosotomy (Fendrich and Gazzaniga 1989, Corballis and Trudel 1993) suggest that interhemispheric co-operation may be needed for effective processing of stimuli presented to the vertical meridian, as performance is better when stimuli are presented lateral to the vertical meridian.

It is currently unclear whether naso-temporal overlap at the vertical meridian forms the basic of macular sparing, but results discussed previously with regards to patients with macular splitting and spared islands of vision in the hemianopic field suggest the two may be separate phenomena. Macular sparing would also afford a small amount of midline disparity registration of approximately 3 degrees, which is key for acute foveal stereopsis, though up to 5 degrees across the vertical meridian is needed for stereoacuity levels of 60 arcsec (Hirai 2002). Macular sparing in hemianopes is a variable phenomenon, with reports of sparing up to 2 - 4^0 after unilateral occipital injury (Zihl 1989, Reinhard 2003), sparing after bilateral occipital injury (Symonds and McKenzie 1957) to no such sparing (Celesia 1983). There is a similar variability in studies of hemispherectomised patients (see section 3.1.3), which suggests that it probably cannot account for all instances of intact midline stereopsis in hemianopes. Another possibility that may account for presence of midline stereopsis in hemianopia is the subtle ipsilesional adjustment of head centred space such that the "midline" stimulus then shifts into the intact visual hemifield (Doricchi 2002). Use of a head restraint or an eye-tracking device ensures that stimuli are always within the central visual field, thus eliminating this as a potential confound. It is acknowledged that such techniques were not used on the current study, thus subtle compensatory head and eye movements are a potential confound.

The quandaries discussed above regarding the mechanisms of midline stereopsis are similarly addressed in studies of blindsight (Stoerig 1996, Fendrich 2001, Ptito 2001). These studies have focused on detection of form (Marcel 1998), colour (Brent 1994, Barbur 1999) and motion within the blind hemifield (Azzopardi and Cowey 2001, Wessinger et al 1999), with a relative neglect of investigating midline stereopsis. Blindsight studies also address the possibility of subcortical pathways mediating visual functions in the blind hemifield (Tomaioulo 1997, Boire 2001). This possibility remains unaddressed in studies investigating stereopsis in hemianopes, perhaps due to anatomical studies illustrating that processing of retinal disparity cues is cortically based.

3.1.2 The development of stereoacuity

Studies examining stereopsis in infants suggest early responses to disparity cues emerge between 3 and 4 months (Birch 2005, Fox 1980, Held 1980). There are several hypotheses relating to the nature of binocular vision in the pre- stereoptic period. Inputs from the two eyes are presumed to be combined non-selectively, thus information pertaining to the eye of origin for a given piece of input is lost at a relatively early stage in cortical visual processing. Loss of this information precludes fusion, rivalry and stereoptic mechanisms, which depend on selective combinations of input from each eye. Data suggest that the pre-stereoptic visual system is sensitive to orientation, number of items, contrast, spatial frequency and colour, without registration of eye of origin. It is assumed that neurones are non-selectively binocular at this stage, becoming progressively monocular or selectively binocular as ocular dominance columns develop (Held 1985). Non-selective pooling of binocular information is replaced by monocular representations, which are recombined for higher level binocular processing which enables comparison of inputs from each eye.

Several pre-requisites for stereoscopic vision have been postulated, including retinal maturity levels sufficient to provide a minimum level of monocular resolution (Aslin 1980) and cortical maturation levels sufficient to preserve information pertaining to the eye of origin and thus provide disparity signals (Held 1991). Crossed disparity tends to emerge before uncrossed disparity (Birch 1982), though it is unclear at present why this is so. Although responses to disparity cues seem to emerge rather suddenly, there is a gradual refinement of the minimum angle of disparity that can be utilised to resolve stereoscopic depth cues throughout early childhood. Studies suggest that coarse binocular function of approximately 400 seconds appears between 3-4 months, with stereoacuity of approximately 1 arcmin emerging between 6-8 months of age (Birch 1982). Adult levels of stereoacuity at 30-40 arcsec are consistently found at around 5:6 years (Tomac 2000, Ciner 1991), though some studies estimate 7 years (Cooper et al 1979) and even 10 years (Alumbrad 2006).

The developmental trajectory described above is critically dependent on accurate acuity and alignment of the visual axes, thus children with anisometropia or strabismus do not develop stereoscopic depth perception. Habitual suppression of one eye results in reduced acuity and contrast sensitivity. Even when a strong fixation preference does not develop, alternating suppression prevents simultaneous experience of input from both eyes and produces permanent impairment in binocular function. Early correction of acuity or surgical correction of misalignment results in improved fusion, with stereoacuity between 60-400 seconds (Birch et al 2004, Fawcett et al 2004), with further improvements brought about by turning the head as discussed earlier. Considering the protracted course of development of acute stereopsis (approximately 5-7 years), and the paucity of literature to date on the impact of unilateral cerebral lesions sustained in childhood and the integrity of stereoscopic vision (Mercuri et al 1996), it is of interest to examine whether cerebral injury sustained during childhood has any bearing on the presence or absence of stereoscopic vision.

3.1.3 Stereopsis after hemispherectomy

There is only one case study that mentions the presence of stereoscopic vision in a hemispherectomised patient to date (Battro 2002). This case was a right hemispherectomised patient with congenital pathology, though no details were given regarding the types of assessments used and scores obtained. Further study is needed to confirm whether stereoscopic vision is generally present after hemispherectomy, and whether factors such as side of hemispheric removal and age at onset of pathology have any obvious significance. Macular sparing has been documented in previous hemispherectomy studies, and there appears to be no obvious advantage of early onset of pathology as hemispherectomised cases with adult onset of pathology may demonstrate macular vision (Bell 1949, Rowe 1937) and cases with earlier onset of pathology may demonstrate hemianopia without macular sparing (Sergent and Villemure 1989, Wessinger 1996).

3.2 Aims and predictions

The principal aims of investigating stereopsis after hemispherectomy were (1) to gain a preliminary impression of the nature and extent of any impairment in stereopsis in hemispherectomised patients and controls; (2) to determine the relationship between side of hemispheric injury and task performance; (3) to determine whether stereopsis is more efficient when mediated by two functional cerebral hemispheres, and (4) to determine if there is a relationship between age at onset of pathology and integrity of stereopsis.

Between groups comparisons of neuropsychological data from the patient and control groups were carried out. The predictions were as follows:

- Performance will be similar in left and right hemispherectomised patients due to symmetrical representation of neural architecture responsible for basic sensory processing.
- Performance will be worse in the patient group due to the presence of hemianopia and ocular misalignment, and associated difficulties resolving disparity cues in the sagittal plane.
- Performance will not be related to age at onset of pathology if the presence of stereopsis is related to macular sparing or head turning. It is possible that a relationship between age at onset of pathology and stereopsis will be present if naso-temporal overlap plays a significant part in midline stereopsis.

3.3 Methods - Stereopsis screening instruments

As there are a variety of monocular cues that signal depth, including size, shadows, linear perspective and figure-ground cues, the integrity of the binocular fusion mechanism must be assessed by tests that control for these variables. The two tests selected for this study are widely used for screening both children and adults. Their appeal with respect to screening children and adults with cognitive impairment is based on the tests being rapidly and easily administered, with only a minimum of specialist equipment required, namely a pair of spectacles with specialised lenses. Additionally, the two tests of stereoscopic vision selected for this study are able to test stereoacuity over a broad range of disparity values ranging from coarse qualitative screening to highly conservative estimates of stereoacuity. Both tests yield a measure of the minimum angle of retinal disparity that can be utilised to perceive depth.

3.3.1 The Titmus Test

The Titmus test (Stereo Optical Co., Chicago, Illinois 1994) consists of three subtests: the stereo fly test, the circle test and the animal test. All stereograms are viewed through polarising lenses at a distance of 40 centimetres. The fly test is a qualitative measure of coarse stereopsis, the fly appearing in depth if the images are fused correctly. The subject attempts to pinch the tip of the wing with the thumb and forefinger. If the fingers remain in front the plane of the stereogram, it can be inferred that the fly is seen in depth. The animals test consists of 3 rows of 5 animals, with one animal in each row having disparity of 400, 200 and 100 arcsec respectively. If disparity cues are registered, the animal will appear in depth, experienced as "coming out of " or "floating above" the page. The circles test screens for stereoacuity between 40 – 800 arcsec. It consists of 9 numbered diamonds, each containing four circles. One of the circles in each diamond has disparity cues, and the subject indicates which of the circles appear out of the plane of the other three.

Despite the appeal of the Titmus test in terms of ease of administration, Cooper (1977) suggests it is possible to use monocular cues to achieve a positive result on the coarse stereopsis items. This is achieved by observing the lateral displacement of the correct image relative to the other images (Simons and Reinecke 1974, Hall 1982). The test may therefore be vulnerable to yielding false positives, despite its widespread use as a screening instrument. To minimise the risks of obtaining false positive results, subjects were tested according to the manual in terms of pointing to relevant stimuli, but were also asked to report the relative depth plane of the stimulus to ensure the stimulus was actually seen in depth and did not merely look somehow different to the other stimuli. Subjects were also asked to close each eye alternately after viewing the stimuli and making responses, to see if the percept altered upon monocular viewing. If a previously positive stimulus reverted to being negative upon closure of one eye, it was assumed that positive results were gained from binocular as opposed to monocular cues.

3.3.2 The TNO Test for Stereoscopic Vision

The TNO test of stereoscopic vision (Walraven 1975) was administered to provide a second measure of stereoacuity. It was the first clinical application of the random dot stereograms pioneered by Aschenbrenner (1954; see Shipley 1971) and Julesz (1962). Previous reports suggest that the TNO and Titmus stereo test correlate well (Shah et al 1995), thus results from the two tests can be compared to confirm or exclude the presence of stereopsis. The TNO test is regarded as superior to the Stereo Fly test in eliminating false positive results, as the design of the test items prevents use of monocular cues, though the TNO is susceptible to underestimation of stereopsis, as the red – green filters have been shown to reduce stereoacuity (Cornforth 1987, Larson 1988). The test consists of seven plates that contain figures that can only be seen when both eyes co-operate to produce disparity cues. Each plate consists of a stereogram in which the half images for each eye have been superimposed and printed in complementary colours (red or green), producing an anaglyph. The images represent two retinal views of a three dimensional scene, and will evoke the perception of an image in depth when presented to each eye separately. The anaglyphs are viewed through red-green filter lenses so that each eye sees only one of the half images. Individuals with deuteranopia or protanopia are still able to complete the task via differences in luminance of the two half images that become evident upon wearing the filter lenses (Walraven and Janzen 1993). The stereogram reproduces the two retinal images that would result from viewing a speckled surface in front of a background of exactly the same texture. Monocular form perception cannot operate as no single retinal image provides sufficient figure-ground information. The hidden figures in the stereograms are registered at slightly different locations in the two retinal images and will thus become apparent only when viewed binocularly. This becomes evident when closing one eye whilst viewing the images with the filter lenses; the hidden figure disappears, only to reappear again when both eyes are open.

Plates 1-3 establish the presence of coarse stereopsis (33 arcmin) via detection of simple shapes and a butterfly. Plate 4 is a binocular suppression test. As it cannot be administered to individuals with hemianopia, it was not included in this assessment. Plates 5-7 are used to quantify the minimum angle of disparity that affords stereoscopic depth perception, with figures ranging from 15 – 480 arcsec. Each plate contains 4 discs in depth, each with a missing sector in one of four positions. The subject is asked if they can see the discs, and to indicate the location of the missing sectors.

The plates were viewed at a distance of 40 cm. If a subject had difficulty seeing the figures, the plates were brought closer at 30 then 20 cm, and disparities were calculated by adjusting for decreased distance: $A = (40/d)^{m}$, where A is the actual disparity, d the viewing distance in centimetres, and m is the original disparity value for the plate as stated in the manual.

3.4 Results

3.4.1 The Titmus Test and TNO Test – patients and controls

Results for the Titmus test are summarised in table 3.1, figure 3.4 and figure 3.5. The number of left vs right and congenital vs acquired patients without stereopsis were approximately equal. The patients that demonstrated some level of stereoacuity were below the conventional cut off level of stereopsis tests of 240 arcsec (Walraven 1975), and demonstrated a similar range of acuities to control subjects.

Table 3.1. Results from the Titmus test – patients and controls (each cell represents number of cases)

Group	No stereopsis	200 Arcsec	100 Arcsec	80 Arcsec	< 80 Arcsec
$HY_{L\ (N=12)}$	6	1	1	1	3
$CT_{L\ (N=11)}$	0	0	2	2	7
$HY_{R\ (N=10)}$	5	0	2	1	2
$CT_{R\ (N=8)}$	0	1	1	3	3
$HYc_{\ (N=11)}$	6	1	2	1	1
$HY_{A\ (N=11)}$	5	0	1	1	4

HY_L = left hemispherectomy group; CT_L = control subjects matched to patients with left hemispherectomy; HY_R = right hemispherectomy group; CT_R = control subjects matched to patients with right hemispherectomy; HYc = hemispherectomy group with congenital, pathology; HY_A = hemispherectomy group with acquired pathology.

All controls demonstrated a level of stereoacuity that was below the conventional cut off level of stereopsis tests. Case **BL$_{CR}$5** had a stereoacuity level of 200arc sec, which is unexpectedly poor, though no strabismus or visual field impairment was noted.

The TNO test appeared to give a more conservative estimate of stereoacuity, with only 7 hemispherectomised patients demonstrating some degree of stereoacuity on this test (see table 3.2. and figure 3.4). Five patients demonstrated stereoacuity levels between 30-60 arcsec as measured in the Titmus test, and 2 cases demonstrating stereoacuity levels of 100 arcsec in the Titmus test had stereoacuity of 120 arcsec in the TNO test. Two of the patients (**PO$_L$2, TB$_R$6**) that obtained positive results on the Titmus test whilst failing to demonstrate stereoacuity on the TNO test were noted to have some difficulty describing the nature of the effect of depth in the Titmus test stimuli, thus the possibility of use of monocular cues must be considered as a source of discrepancy between the two test results. Of the remaining two patients with positive Titmus test results but negative TNO test results, case **HW$_L$6** made some attempt at fusion, describing patches of "floating dots" in locations appropriate to hidden figures in plates 1-3, but was unable to fully resolve the identity of the stimuli. Case **SN$_R$5** resolved one of two circles on plate 2 and named the inverted triangle in plate 3 as "possibly heart shaped". Absolute difficulties in shape discrimination for these cases were ruled out due to adequate naming of shapes in the colour vision test used when screening all research participants prior to taking part in the study.

Table 3.2. Results from the TNO – patients and controls (each cell represents number of cases)

Group	No stereopsis	240 Arcsec	120 Arcsec	< 80 Arcsec
$HY_{L\,(N=12)}$	8	0	1	3
$CT_{L\,(N=11)}$	0	1	3	7
$HY_{R\,(N=9)}$	6	0	1	2
$CT_{R\,(N=7)}$	0	2	2	3
$HYc_{\,(N=11)}$	8	0	2	1
$HY_{A\,(N=11)}$	7	0	0	4

HY_L = left hemispherectomy group; CT_L = control subjects matched to patients with left hemispherectomy; HY_R = right hemispherectomy group; CT_R = control subjects matched to patients with right hemispherectomy; HYc = hemispherectomy group with congenital, pathology; HY_A = hemispherectomy group with acquired pathology.

The phenomenon of incomplete resolution of the stimulus in the presence of some evidence of fusion was also noted in case **JL $_L$12**, who detected missing sectors of discs in plate 7 with disparity cues of 30 arcsec, but could only detect the vague presence of something floating without resolution of its shape when viewing the 15 arcsec discs. The TNO test also appeared to give a more conservative estimate of stereoacuity in controls. Deuteranopic control participant **GB$_{CR}$1** refused to do the TNO test owing to the red-green nature of the stimuli, hence results from case **PP$_R$1** were omitted from group comparisons for this test.

Figure 3:4. Stereoacuity scores – patients.

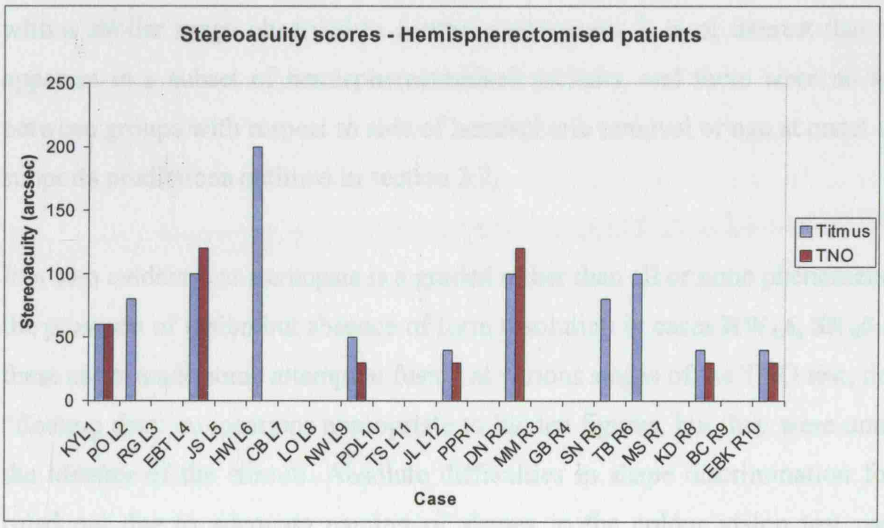
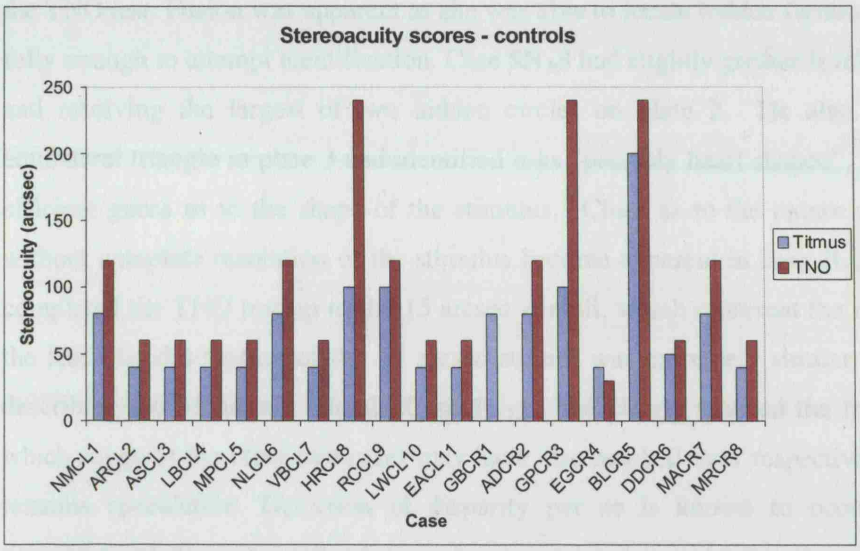


Figure 3:5. Stereoacuity scores – control subjects



Pearson correlations did not reveal an association between stereoacuity levels and IQ scores (VIQ, PIQ, FSIQ) for either hemispherectomised patients or controls, suggesting that cognitive impairment is unlikely to result in low stereoacuity scores in these two tasks.

3.5 Discussion

3.5.1 Integrity of stereopsis after left or right hemispherectomy

Overall, the results suggest that it is possible for the isolated left and right hemispheres to resolve disparity cues contained within standardised tests of stereoscopic vision. Stereoacuity scores obtained by hemispherectomised patients ranged between ranged between 40-240 arcsec, with a similar range observed in control participants. It is of interest that stereopsis was only apparent in a subset of hemispherectomised patients, and there were no apparent differences between groups with respect to side of hemispheric removal or age at onset of pathology, which supports predictions outlined in section 3.2.

It is also evident that stereopsis is a graded rather than all or none phenomenon, as illustrated by the presence of fusion but absence of form resolution in cases **HW$_L$6, SN$_R$5** and **JL$_L$12**. Each of these cases made some attempt at fusion at various stages of the TNO test, describing patches of "floating dots" in locations appropriate to hidden figures, but they were unable to fully resolve the identity of the stimuli. Absolute difficulties in shape discrimination for these cases were ruled out due to adequate naming of shapes in the colour vision test used when screening participants during recruitment. These findings accord with the hemianopic patient described by Cowey (2000), who also demonstrated some evidence of fusion without being able to identify the stimulus, despite intact shape naming abilities. Case $\mathbf{HW_{L}6}$ had relatively little success on the TNO test. Fusion was apparent as she was able to locate hidden figures but not resolve them fully enough to attempt identification. Case $\mathbf{SN_{R}5}$ had slightly greater levels of success, locating and resolving the largest of two hidden circles on plate 2. He also located the inverted equilateral triangle in plate 3 and identified it as "possibly heart shaped", which represented an efficient guess as to the shape of the stimulus. Clues as to the nature of disparity detection without complete resolution of the stimulus become apparent in case $\mathbf{JL_{L}12}$, who successfully completed the TNO test up to the 15 arcsec stimuli, which represent the most difficult level of the test. His description of the 15 arcsec stimuli was extremely similar to case $\mathbf{HW_{L}6}$ when describing the 33 arcmin stimuli. Case $\mathbf{JL_{L}12}$ had clearly reached the limit of his resolution, which suggests the other two cases may have also reached their respective limits, although this remains speculative. Detection of disparity per se is known to occur before subsequent perception of disparity defined form in extrastriate areas, hence perception of depth within random dot stereograms (Julesz 1986). It is possible that a given level of input is required before disparity information can be resolved in extrastriate areas that provide information pertaining to edge in V2 and shape in V4. Ringach (2003) provides evidence for gradual resolution of progressively finer spatial scales when resolving binocular disparity cues, such that computation of coarse levels of disparity builds the foundation for fine scale computations. Relatively weak input at the limits of an individual's disparity threshold may provide insufficient input for resolution of contours that go beyond simple edge detection, and serves to illustrate the stepwise process of resolving disparity information.

3.5.2 Comparison of left versus right hemispherectomised patients

Reports of right hemisphere dominance for stereopsis (Durnford and Kimura 1971, Ptito 1993, Kwee 1999, Fortin et al 2002, Nishida et al 2002) are not supported by results from this study. There were no differences in the number of left and right hemispherectomised patients demonstrating stereopsis, as illustrated in tables 3.1 and 3.2. Statistical analysis was omitted as it was clear that exactly the same proportion of patients in each group demonstrated stereopsis. Half of each hemispherectomised subgroup (left, right) demonstrated stereopsis on the Titmus test, and a third of each hemispherectomised subgroup (left, right) demonstrated stereopsis on the TNO test. Positive results confirm for the first time that either isolated hemisphere is capable of mediating stereopsis, which accords with anatomical and neuroimaging studies described in section 3.1.1 that suggest either hemisphere has the necessary architecture for resolving binocular disparity cues.

3.5.3 Stereopsis with one versus two cerebral hemispheres

Results from stereoacuity tests reveal striking differences between patient and control groups. Whilst all controls demonstrated some degree of stereoacuity, only 7 of 22 hemispherectomised patients were able to resolve disparity cues on both tests. Although results from the control group suggest that cognitively impaired children and adolescents are able to achieve stereoacuity scores at or below the pass-fail criterion of 240 arcsec set by the tests used, all participants were above the age at which stereoacuity reaches adult levels of approximately 40 arcsec. In fact only half of control participants achieved this level of acuity. None of the controls had strabismus or any known visual field impairments, which suggests that factors other than visual field integrity and gross ocular alignment may influence stereoacuity scores. In contrast to previous studies (Green 1977, Gamio 2003), cognitive impairment did not appear to be associated with low stereoacuity scores in either hemispherectomised patient or control groups, though it is acknowledged that only IQ scores were used to test the association.

Ocular misalignment and visual field defects are of crucial importance when examining results from hemispherectomised patients, as discussed in section 3.1. It is of note that 7 of the 13 hemispherectomised patients that did not reliably demonstrate stereoscopic vision had unilateral exotropia, thus precluding stereopsis. As strabismus was documented by clinical observation, and only binocular acuity was measured in patients and controls due to reluctance of participants to cover an eye to engage in monocular testing, it remains possible that microtropia and anisometropia may account for the six patients that did not demonstrate stereopsis despite an apparent lack of strabismus. It is also possible that midline stereopsis cannot occur within an isolated hemisphere due to lack of interhemispheric co-operation for stimuli situated proximal and distal to the horopter (Jeeves 1991). Hemispherectomised patients that do not engage compensatory mechanisms in the form of head and eye movements to shift the stimulus into the intact hemifield would therefore fail to resolve disparity cues for centrally presented stimuli. As head and eye movements were not strictly monitored in this pilot study, a firm conclusion cannot be made. Further study using more stringent control measures will help to clarify these issues.

It must be acknowledged however, that 11 patients did demonstrate stereoscopic depth perception. Assuming that cognitive impairment, ocular alignment and visual acuity are not providing an obstacle, three factors addressed in section 3.1 may be of some importance with respect to midline stereopsis in hemispherectomised patients. Macular sparing, shift of headcentric space and aberrant connectivity in the form of naso-temporal overlap may each contribute to the presence of stereopsis. All hemispherectomised patients in this study had a homonymous hemianopia contralateral to the side of hemispheric removal, and macular sparing was not evident on perimetry. Macular sparing cannot be ruled out however, as accurate visual field mapping of cognitively impaired children and adolescents is extremely difficult (Harding 2002, Spencer 2003), hence macular sparing or islands of residual vision may be missed on perimetry. Even when conventional perimetry has been successful and demonstrates complete loss of a visual hemifield, measurement within 3 degrees of the vertical meridian can only be approximated (Hirai 2002). This narrow zone of midline sparing may facilitate disparity detection for stimuli that are subject to foveal fixation, and may contribute to stereoacuity in these patients. This also accords with the lack of a distinct relationship between age at onset of pathology and presence of stereopsis, as macular sparing may be observed after hemispherectomy in adult onset cases (Rowe 1937). It is difficult to reconcile macular sparing with acute levels of stereopsis however, as stereoacuity levels of 60 arcsec require an island of vision of 5 degrees across the vertical meridian, which is beyond the range that macular sparing affords. Four hemispherectomised cases demonstrated stereoacuity of less than 60 degrees, which suggests that factors other than macular spring may afford stereopsis in these patients. It is most likely that a combination of factors interacts to afford stereopsis after hemispherectomy, and these may differ across individuals.

As discussed earlier (section 3.2.1), stereopsis is possible in hemianopic patients if at least one of the images is eccentric to the sagittal plane of the fixation point. Turning the eyes or the head could displace the fixation point from the conventional midline into the sighted hemifield, thus increasing the probability of 2 points falling within sighted hemiretinae and subsequent registration of binocular input for detection of disparity. As subjects wore spectacles when engaged in the stereoacuity tasks, it was not possible to directly observe eye position to confirm whether this strategy was being used. Upon questioning, none of the patients were acutely aware of using such a strategy, though it does not preclude the possibility of its use. It is acknowledged that lack of control for head and eye movement is a potential limitation of this study, though it was deemed appropriate to introduce these new stimuli to participants non intrusively, with a view to designing a more controlled paradigm for subsequent testing sessions upon obtaining positive results. Results from the current study could then be used to determine whether unrestricted head movements contribute to binocular depth perception in these patients.

3.5.4 The relationship between age at brain injury and presence of stereopsis

The possibility of naso-temporal overlap via crossed temporal and uncrossed nasal projections at the vertical meridian may contribute to midline stereopsis as discussed in section 3.1, though it is unclear as to why some patients would appear to derive benefit from this and not others. Although animal studies suggest that early injury is associated with greater naso-temporal overlap (Bunt 1977, Leventhal 1993), it remains to be seen why hemispherectomised cases with congenital disease are no more likely to demonstrate stereopsis than patients with acquired disease. Case **JL $_{L}$12** developed Rasmussen's encephalitis aged 10:0 and underwent surgery aged 11:9, yet stereopsis is preserved. Similarly, case **EBK $_{R}$10** also has preserved stereopsis after acquiring Rasmussen's encephalitis aged 8:1 and having surgery aged 15:1. These findings do not accord with naso-temporal overlap providing a sole mechanism for preserved stereopsis after hemispherectomy, but it remains possible that patients with early injury may derive benefit from such projections.

3.5.5 Summary

In summary, all control participants and 7 of 22 hemispherectomised patients demonstrated some level of stereoacuity on both screening tests, with a similar range of acuities in both groups. No laterality or age at injury effects were observed, which accords with literature suggesting that basic visual functions are established early and are bilaterally represented. Possible reasons for stereoacuity being absent in patients or poorer than expected in controls include monocular suppression due to ocular misalignment or anisometropia, or reduced levels of fusion due to milder forms of these two conditions. Whilst an isolated cerebral hemisphere is capable of stereopsis when corresponding points are outside the sagittal plane, possible factors increasing the probability of midline fusion include macular sparing permitting some degree of fusion within the midline, altering the conventional point of fixation by turning the head and eyes, and naso-temporal overlap at the vertical meridian. Further study may help to elucidate the relative significance of these factors with respect to increasing the probability of midline stereopsis.

4 Visual attention

4.1 Introduction

Visual attention is a multifaceted construct that involves co-ordinated feed forward and feedback activity across dedicated neural networks to ensure continuous and relevant stimulus selection within complex visual scenes. This enables efficient interpretation of the visual scene despite limited processing capacity. Theoretical models that outline the various functions involved in visual attention are presented in this chapter along with their related anatomical underpinnings. Cerebral laterality issues are addressed in addition to the developmental trajectory of attentional function as a prelude to investigating the integrity of a working model of visual attention in hemispherectomised patients. Line bisection and visual search tasks are used to examine spatial awareness and selective attention in these patients and their controls.

4.1.1 Defining attentional function

Visual attention is a vast and complex domain of cognitive function. It was summarised by James (1890) as

"... the taking possession by the mind, in clear and vivid form, of one out of what seem several simultaneously possible objects or trains of thought. Focalisation, concentration, of consciousness are its essence. It implies withdrawal from some things in order to deal effectively with others, and is a condition which has a real opposite in the confused, dazed and scatterbrained state"

A more contemporary metaphor is that of a zoom lens (Murphy and Eriksen 1987), that initially covers a wide area of visual field allowing parallel processing of stimuli at coarse resolution. Initial scene processing and gross discriminations are possible at this level via simple clustering of visual features, which may eventually be replaced with progressively narrower distribution of attention if higher resolution is needed such as that required for individual object identification in a cluttered array, and registration of its component features. In this manner, the elements of a scene are grouped in successively finer spatial scales as the attentional focus is narrowed and intensified.

This proposed mechanism of attentional focus has implications for the visual search process, as when a broad attentional field is employed, the search field is covered rapidly by execution of large saccadic eye movements. The gain in speed results in reduced accuracy as spatial attention is thinly spread hence targets are missed. Smaller attentional fields are optimal for target detection, but the search is considerably slower, more fixations are required and there is a risk of forgetting where one has already searched. The burden on spatial working memory can be reduced whilst still executing an efficient search by adopting a search strategy that has a predefined systematic form that may be adopted relatively easily and with little mnemonic effort. Circular and rectilinear paths are typically employed (Mort and Kennard 2003). Such strategies are not fixed but dynamic processes that can be adjusted as the requirements of the search evolve, such as re-checking for missed targets.

4.1.2 Treisman's feature integration theory

Subsequent processing of attended stimuli is summarised in Treisman's feature integration theory (Treisman and Gelade 1980, Treisman 1998), which provides a more elaborate account of the zoom lens metaphor. Whilst there are shortcomings to the theory in terms of the pre-attentive nature of parallel search (Joseph et al 1997, Rock et al 1992) and the exclusively serial nature of making conjunctions (Chelazzi 1993, Duncan 1995), the model illustrates the role of selective attention in target identification within a cluttered array, and differentiates between attentional demands placed by different target-distractor arrays.

The model proposes that during early visual processing, parallel extraction of simple local properties of a scene such as outlines and orientation can result in recombination to object representations by attending to the location of the features of a particular object. Attention "glues" features together from separate feature maps in this respect. When attentional resources bind features into a coherent stimulus, a temporary object file is created that can be compared to stored representations, thus enabling target detection and recognition. This is useful in visual search tasks where the target is situated amongst distractors. Simple visual discriminations where target and distractor differ by a single salient feature occur rapidly and without effort, as the targets appear to "pop out" from the array. Activation from a single feature map is thus sufficient to detect the target. Whilst parallel or "pop out" searches place some demands on attentional resources, these demands are minimal compared to serial searches. The latter type of search takes place when the target and distractor are harder to differentiate due to a conjunction of features specifying the target, with selective attention applied serially to each item in the array. Support for focal attention being involved in binding of multiple features is demonstrated by the phenomenon of illusory conjunctions whereby constituents of simultaneously presented objects may be erroneously combined (Prinzmetal et al 1986, Cohen and Rafal 1991, Treisman 1998). Illusory conjunctions occur when focal attentive processing is prevented by using brief exposure times, or simultaneously presenting a secondary task that demands focal attention. Recent criticisms of Treisman's model are centred on the over simplification of the attentional search process, as the dichotomy of pre attentive parallel and effortful serial search does not accord with a wealth of literature that suggests even pop out search may be vulnerable to the number of items in an array (Wolfe et al 1992, Verghese and Nakayama 1994), and rapid conjunction searches can proceed independently of the number of items in an array (Nakayama and Silverman 1986, Duncan and Humphreys 1989). It is also apparent that pop out search is compromised when attention is focused on another task such as letter identification (Joseph et al 1997, Rock et al 1992).

More recent models of attention (Chelazzi 1993, Wolfe 1989, 2004) propose that ongoing parallel search processes enable attentional resources to be directed to the most likely location of targets, as opposed to laborious feature by feature search. The conjunction search, whether exclusively serial or inclusive of parallel input, operates over a narrower attentional focus and is thus is more detailed, operates more slowly and places heavier demands on attentional resources due to greater need for top down priming or biasing of the feature processing units involved. This implies that featural and conjunction search may not be qualitatively different, instead representing different ends of a spectrum regarding involvement of attention in visual search as task difficulty increases. In short, whilst there are shortcomings to Treisman's model, it provides a useful working definition of attentional function as applied to visual search, facilitating investigation of performance in simple and conjunction searches and the significance of target:distractor ratio in visual search.

4.1.3 Posner and Petersen's model of visual attention

Whilst the aforementioned models describe feature extraction and analysis during visual search, Posner and Petersen (1990) proposed a model that addressed the dynamic act of visual search; namely disengaging from ones current area of focus and shifting attention by orienting to new stimuli, disengaging once perceptual analysis is completed to the new location and so on, maintaining vigilance until the search is completed. Attention thus consists of separate but interactive systems that are concerned with different elements of attentional function. The authors proposed a tripartite model that consists of a multimodal orienting network that is responsive to spatial and non spatial attributes of stimuli, an arousal mechanism that maintains vigilant search and an executive control network that is involved in error monitoring, target detection, inhibition of automatic responses and resolving conflict. The authors provide a comprehensive account of the anatomical underpinnings of the model, which are described in section 4.1.4. Orienting is defined as the selection of sensory information, which may be overt when the eyes are directed towards an area of interest, or covert, whereby a spatial area is prioritised without moving the eyes towards it. Posner describes the process of orienting to a stimulus in a new location as a disengagement from the current location, an attentional movement to the new area of interest and an engagement at the target location. This selective direction of visual attention towards a location is otherwise known as spatial attention. Orienting is crucial for ensuring foveation of relevant areas of the visual scene and therefore efficient extraction of stimulus attributes. Vigilance is similarly important, as it sustains alertness and reduces the probability of processing irrelevant information and keeps an individual focused on the task at hand. Vigilance and executive control interact to modify responses after errors, and to maintain efficient goal directed search (Callejas et al 2004).

4.1.4 The anatomy of visual attention

The neural architecture responsible for visual attention is often described as a collection of networks that traverse different brain regions and affect top down priming, orienting, target identification, vigilance and executive control. Posner's model has been substantiated by studies that have defined the associated neural substrates of each of the three components (Corbetta 1998), and the feature integration theory has benefited from anatomical correlations from neuroimaging studies (Corbetta 1995, Vandenberghe 1997).

Anatomical underpinnings of the feature integration theory were not made explicit originally, although feature maps coincide with known properties of cells in striate and extrastriate cortices in terms of retinotopically organised groups of cells with selectivity for colour, orientation, motion and depth (Livingstone and Hubel 1988). In this manner, early parallel extraction of features across the visual scene is a credible starting point, and accords with neuroimaging studies demonstrating feature specific striate and extrastriate activation during early visual processing (Zeki et al 1991, Posner and Gilbert 1999). Neglect of top down priming of early parallel extraction in Treisman's model is exposed by studies demonstrating enhanced activity in stimulus or location relevant areas of cortex in selective attention tasks when a target or location has been pre-specified (Beauchamp 1997, Buechel 1998, O' Craven et al 1999). Microelectrode recordings from cortical cells in non human primates mirror these findings. These studies suggest that response properties of cells in V1-V5 are selectively enhanced when monkeys search for targets that include features such as colour, orientation or motion (Motter 1993, Spitzer 1988, Luck 1997).

Subsequent binding of multiple features has been associated with bilateral parietal lobe activation in PET (Corbetta et al 1993, 1995, Vandenberghe 1997) and fMRI (Kanwisher and Wojciulik 2000, Perry and Zeki 2000, Sturm et al 2006) studies. Levels of activation in parietal regions during this type of search were higher than those requiring only single feature search, suggesting stronger parietal involvement when tasks are more complex. Further support for Treisman's model is provided by reports of patients with occipito-parietal lobe damage that demonstrate an increased tendency towards illusory conjunctions (Friedman-Hill et al 1995, Bernstein and Robertson 1998). In brief, these findings suggest that parietal and striate-extrastriate regions interact to ensure rapid and efficient identification of targets from the visual scene. The parietal lobe is also believed to be important for disengaging attention from a current focus, with midbrain structures moving attention to the new focus, as stipulated by goal directed information from the frontal lobes (Tipper et al 1994). Indeed, patients with parietal lobe damage have difficulty disengaging from stimuli within the ipsilesional hemifield (Posner 1988), despite adequate sensory processing capabilities within the contralesional hemifield. Similarly, patients with damage to the superior colliculus have difficulties shifting attention to the relevant area of visual space (Fernandez-Duque and Posner 2001).

The orienting network in Posner and Petersen's model includes retino-collicular (automatic) pathways for reflexive orienting to rapid onset peripheral stimuli, and a relatively complex voluntary orienting network involving efferent projections of the inferior parietal lobule (IPL) to the superior colliculus and frontal eye fields (Barbas 1981, Pandya 1969, Posner and Peterson 1990, Corbetta et al 1998, 2002). This ensures salient aspects of the environment will be subsequently foveated, as primate studies suggest that both these areas are related to saccade generation (Schiller 1972, Robinson 1969, 1972, Wurtz 1972). Further evidence for an automatic and voluntary orienting system comes from clinical studies, as patients with frontal lobe injury can encounter difficulties with producing voluntary saccades (Ladavas 1997), whereas patients with mid brain lesions had difficulties producing reflexive saccades (Pierrot-Deseilligny et al 1991).

The notion of a putative noradrenergic network in the right hemisphere was introduced in chapter one (section 1.3.1) and was linked to attentional function. The arousal mechanism that contributes to sustained attention in Posner and Peterson's model is a noradrenergic network involving extensive interconnections between the locus coerulus, limbic structures, thalamic nuclei and cortical areas, particularly right fronto-parietal cortices (Fernandez-Duque and Posner 2000). This network enables potentiation of primary sensory areas within the cortex, leading to enhanced efficacy of responses which manifest as faster reaction times, increased target detection rates, and sustained vigilance during cognitive tasks. Evidence for this network in humans comes from neuroimaging studies demonstrating right fronto-parietal activation during states of vigilance (Pardo et al 1991, Coull et al 1996), and noradrenergic antagonists decreasing vigilance (Smith and Nutt 1996). Further support comes from lesion studies. Patients with right frontal (Rueckert and Grafman 1996) or parietal lobe (Posner 1987) damage have difficulty sustaining attention in target detection tasks.

Executive control is a vast, often poorly defined construct that is linked to a network involving the anterior cingulate gyrus, supplementary motor area, the dorsolateral prefrontal cortex and the basal ganglia (Fernandez-Duque and Posner 2001), which is supported by neuroimaging studies demonstrating activation in anterior cingulate and left prefrontal areas during tasks requiring executive function (Cabeza and Nyberg 2000). The structural components of this network reflect its proposed role in the control of goal directed behaviour, target detection, error detection and inhibition of automatic responses. Clinical studies support these assertions, as patients with frontal lobe injuries encounter difficulties with goal directed behaviour (Umilta and Stablum 1998), response modifications and error monitoring (Robertson et al 1997). Right frontal lobe injuries have also been implicated in attentional neglect of the left visual hemifield (Maeshima et al 1994, 1995).

Collectively, this section has shown that visual attention involves cortical activation in a distributed network of fronto-parietal areas that appears to bias response properties in sensory brain regions coding target stimuli. This in turn, modulates subsequent target processing in the visual cortex (Hopfinger 2001). In addition, subcortical and cortical orienting mechanisms have been specified, along with putative networks subserving vigilance and executive function. In short, visual attention requires co-operation and co-ordination within a vast network of anterior and posterior brain regions, hence focal damage may have disastrous consequences if it intersects these networks. Whilst the consequences of focal lesions have been mentioned with respect to different elements of attentional function, an important related issue is whether the left and right hemispheres make unique contributions to attention, an issue that has been addressed in behavioural, neuroimaging and clinical studies.

4.1.5 Laterality issues

Bilateral cortical activation in neuroimaging studies of visual attention (Matsuda et al 2004, Thiel et al 2004) suggests that fronto-parietal networks subserving attention are active in both hemispheres, which implies either hemisphere may be capable of mediating attentional function. This is further substantiated by report of enhanced performance when different stimuli are presented to each visual hemifield for both tracking (Alvarez and Cavanagh 2005) and discrimination tasks (Kraft et al 2005), which suggest information may be processed in parallel within each hemisphere. Although bihemispheric mediation of visual attention is likely, it remains possible that the left and right hemispheres may operate with different levels of efficacy. There have been consistent reports of right hemisphere dominance in conjunction search (Corbetta 1995, Vandenberghe 1997) and vigilance tasks (Pardo 1991, Coull et al 1996). There is also a substantial amount of work that addresses laterality issues in spatial awareness. Although adults can allocate spatial attention more or less equally to left and right hemispaces, there are consistent reports of a right hemisphere and thus left hemispace advantage for processing visual stimuli. This is exemplified in studies of the anatomical underpinnings of attention that illustrate preferential involvement of right fronto-parietal areas as evidenced in neuroimaging studies (Nobre 2001, Corbetta 1993, 95, Vandenberghe 1997), TMS studies that claim normal functioning of the right posterior parietal cortex is necessary for effortful search tasks (Ashbridge 1997) and the phenomena of pseudoneglect (Bowers and Heilman 1980, Dobler 2001, Jewell and McCourt 2000). Pseudoneglect refers to the small but consistent leftward bias observed when adults manually bisect centrally presented lines. The absence of rightward deviation when using the right hand in adults is supportive of callosal transfer of perceptual representations from the right hemisphere providing a small bias towards the left hemispace, which suggests the attentional bias towards the active right hand is overridden by callosal transfer of right hemisphere perceptual representations that create a bias in the left hemispace (Heilman et al 1984). Further support for this assertion comes from the re-appearance of symmetrical neglect in patients with callosal damage, thus unmasking movement influences on visual attention (Heilman 1984, Kashiwagi 1990, Corballis 1995). Symmetrical neglect (see section 4.1.5) refers to small but consistent leftward biases in line bisection when using the left hand, and rightward biases when bisecting with the right hand. It is commonly observed in children up to 13 years of age (Hausmann et al 2003) and is thought to reflect callosal immaturity. Collectively, these observations suggests that the integrity of the right hemisphere is necessary to enable perceptual and attentional functions to override the influence of motor actions that predominate in the right hemispace in the majority of individuals.

Several authors suggest that the left hemisphere is concerned almost exclusively with mediating attention in the right hemispace, whereas the right hemisphere appears to be capable of directing attention to both sides of space, though it favours the left hemispace (Heilman 1979, 1980, Mesulam 1981). Although damage to either hemisphere can result in altered attentional gradients that favour the ipsilesional space, the most profound examples of attentional deficits are predominantly observed after damage to the right hemisphere in both adults (Stone 1991, 1992) and children (Ferro 1984, 1990, Manly 1997). Cases with similar deficits as a result of left hemisphere damage are included in the literature, but they are generally less severe and more transient (Chain 1979, De Renzi 1970, Gainotti 1972, Oxbury 1974, Manly et al 2005). It seems that neglect of the right visual hemifield is more likely to occur after bilateral as opposed to unilateral lesions (Weintraub et al 1987, 1996).

Hemispatial neglect is an acquired cluster of symptoms characterised by a failure to orient, report or respond to stimuli located in one hemispace. It is usually detected and measured along the horizontal plane, but neglect within vertical and radial axes have also been documented

(Rapcsak 1988, Shelton 1990, Vuilleumier 1998). Neglect is typically reported in adult patients with right parietal lobe damage, but occasional cases with right frontal lobe (Maeshima 1994, 1995), bilateral parieto-occipital (Rapcsak 1988, Weintraub 1996), subcortical (Graveleau 1986, Ferro 1987) or callosal lesions (Kashiwagi 1990) have also been reported. Reports of paediatric cases are comparatively rare, perhaps due to more rapid recovery, or involvement of visual field impairments appearing to account for neglect type symptoms (Ferro 1990). Reported cases show similar impairments to adult cases (Ferro 1984, Johnston 1986, Thompson 1991, Laurent-Vannier et al 2003) and damage the right hemisphere was implicated in almost all of these cases. There are other reports however that suggest damage to either hemisphere in childhood may result in contralesional neglect (Schatz et al 2004, Trauner 2003, Katz et al 1998). Recovery from neglect phenomena was rapid in most cases, ranging from hours to months, though it must be acknowledged that more detailed investigations in adult patients have revealed subtle persistent deficits in spatial awareness despite apparent recovery (Robertson 1993, 1999). There are several explanations for neglect phenomena, including failure to disengage from a target in the intact field (Posner 1990), competitive inhibition from the intact hemisphere (Duncan 1996, 1997) and anisometry of mental representation of left and right hemispace (Bisiach 1998). Tests used to measure the severity of the spatial deficit include line bisection, cancellation tasks and drawing. Consequently, these patients show characteristic profiles such as rightward deviations of line bisection and omission of targets or features in the left hemispace when completing cancellation or drawing tasks respectively. Neglect may be reduced if movements of the contralesional hand are permitted within the contralesional hemispace, suggesting intimate connection between spatial awareness and motor action, with attention being biased towards the active hand.

A recurrent problem in studies of patients with focal cerebral lesions relates to precise localisation of lesions and their effects on adjacent intrahemispheric regions and their homologous counterparts in the opposite hemisphere. Studies of callosotomy patients have provided valuable insight into hemispheric asymmetries in attentional function. It becomes apparent that either hemisphere is able to mediate attentional tasks (Reuter-Lorenz and Fendrich 1990, Luck 1989, Corballis 1995), though callosotomy patients may demonstrate right hemisphere superiority in attention tasks that manifest as increased vigilance and faster reaction times (Dimond 1976, 1979, Corballis 1995). Further support for both hemispheres being capable of visual search and target selection comes from callosotomy studies that demonstrate faster visual search times when the search field is presented to both hemispheres as opposed to presenting the array to a single hemisphere (Luck 1989). It is of note that the disconnected left hemisphere does not appear to neglect the left side of space (Plourde and Sperry 1984, Corballis 1995 but see Kashiwagi et al 1990), which suggests that lack of competition from the intact hemisphere after callosotomy enables the damaged hemisphere to direct attention toward the contralesional hemispace (Duncan 1996, 1997). An opposing view is that neglect associated with focal unilateral lesions may be associated with inhibition of compensatory abilities in the intact hemisphere by default engagement of the damaged region in the opposite hemisphere (Heilman 1984). Further study of spatial awareness of the isolated left and right hemispheres is needed to explore these possibilities.

4.1.6 The development of visual attention

There appears to be a developmental trajectory in attentional function that enables the emergence of voluntary, cortically based functions whilst preserving the functional integrity of reflexive subcortical mechanisms present in the first few months of life. Neonates display both non-specific orienting, and attention to salient visual stimuli. Early, predominantly retino-collicular orienting and fixation mechanisms in the form of reflexive saccades become increasingly constrained within the first six months of life by cortically based attentional mechanisms (Plude 1994). The emergence of voluntary saccades is believed to reflect activity of areas V1, V2, V4, parietal and frontal cortices, signalling the ability to disengage attention and to shift to a novel stimulus, even in the presence of a strong central attractor, thus illustrating the ability to "narrow" the zoom lens of attentional function. Smooth pursuit mechanisms become established within the first two years of life (Richards 2003), completing the necessary repertoire of occulomotor functions necessary for orienting and tracking stimuli that enable subsequent foveation and registration of relevant attributes of the visual scene.

Development of alert, vigilant, sustained attention occurs by the end of the second year, with executive type functions such as inhibition of inappropriate responses and facilitation of correct responses becoming apparent in the third year of life (Richards 2003). The basic elements of Posner and Petersen's model of attentional function are therefore present at 3 years of age. Studies addressing attentional function in later childhood suggest that attentional processing becomes faster and more efficient with age (Lin et al 1999). Wright and Vlietstra (1975) suggest that there is a transition in early childhood from random exploration, controlled by salient features of stimuli, to systematic search that becomes more logical and goal directed. In this manner, it is likely that the development of efficient selective attention precedes and is necessary for later development of other components of attentional function incorporating increased input from executive systems and greater vigilance. This is exemplified in McKay's (1994) study, which suggests that sustained, selective and executive attentional processing have separate developmental trajectories, with response organisation as a measure of executive function becoming systematic and efficient in the majority of children aged above 9 years, whereas selective attention measures demonstrated high levels of efficacy at 7 years of age.

Sustained attention demonstrated rapid development between 11 years of age and adulthood, reflecting maturation of the ability to employ task relevant attentional resources over prolonged periods.

One factor that is believed to contribute to improved attentional function during development is callosal maturation (Rueckert 1994), which enhances efficient information exchange and thus division of labour between the hemispheres when task demands increase beyond the capacity of unihemispheric processing. Belger and Banich (1998) suggests that the ability to perform operations in parallel across the hemispheres leads to a performance advantage in selective attention tasks, perhaps as a result of decreased interference between processes that are employed to mediate the task at hand. The inability to divide labour across the two hemispheres would manifest when task demands exceeded that which may be subserved by a single hemisphere. The concept of callosal contributions to attentional function also has direct relevance to hemispherectomy patients, where lack of callosal transfer may result in attentional difficulties relative to individuals with two functional hemispheres. Indeed, the concept of division of labour is supported by studies of callosotomy patients (Belger and Banich 1998) and neurologically intact individuals (Alvarez and Cavanagh 2005) whereby complex tasks are more easily accomplished by presenting different components of the task to separate hemispheres. Further support for this assertion comes from children with attentional difficulties that demonstrate reduced callosal efficiency (Rueckert et al 1996, Hynd 1991).

A related observation during development is the decoupling of attention from motor activity as reported in simple line bisection tasks. Neurologically intact children tend to demonstrate symmetrical neglect (see section 4.1.5), which is attributed to callosal immaturity rendering spatial representation vulnerable to current motor activity (Bradshaw 1988, Dellatolas 1996, Dobler 2001). Conversely, a slight majority of neurologically intact right handed adults show a leftward bias when bisecting centrally presented horizontal lines (McCourt and Jewell 1999, Hausmann 2003). This "pseudoneglect" effect is amplified when the left hand is used (Schenkenberg 1980, Scarisbrick 1987), and when lines are positioned to the left of the midline (Hausmann 2003). Evidence for pseudoneglect in adults is mixed however. Nichelli (1989) and Nielsen (1999) found that neurologically intact adults show a centripetal bisection bias for lines displaced to the left and right of the midline, whilst other studies report no consistent bias in bisecting lines (Shelton 1990, Halligan 1990, Manning 1990). The shift from symmetrical to pseudoneglect and thus hand specific effects to hand independent effects is thought to occur between 10-13 years of age (Dellatolas 1996, Hausmann 2003), which coincides with age at which line bisection is mastered (Van Vugt 2000). This suggests that development brings increasing independence from action to the visual attentional system, perhaps due to callosal maturation and consequent predominance of right hemisphere mediation of spatial attention resulting in marginally increased deployment of resources to the left hemispace. Indeed, symmetrical neglect is attenuated when lines are positioned to the left of the midline, with younger subjects making small leftward deviations with the right hand as opposed to strong rightward biases with central and rightward lines. Although bisection biases exist in children and adults, they are often minimal, approximating 2mm. Dobler found that mean bisection errors to the left and right in 6:6-7:6 year olds were approximately 1.5-3.5mm (1.5-3.5% of half length).

It becomes clear that results from bisection tasks are inconsistent, though in general, children under the age of 10 years seem to demonstrate a centrifugal bias in bisection according to which hand is used and displacement of lines from the midline, whereas adults demonstrate a small but reliable leftward deviation that is independent of left or right hand use and spatial displacement of lines from the midline.

4.1.7 Attentional function after hemispherectomy

There are no reported cases of neglect to date in hemispherectomy patients, which is particularly interesting in terms of patients that are functioning without a right hemisphere. It is acknowledged however that there are few studies that document attentional function after hemispherectomy, and patients are tested after substantial recovery periods, which reduce the likelihood of detecting neglect type symptoms. The possibility also remains that the presence of hemianopia may have deterred detailed assessments of spatial awareness due to inherent difficulties separating neglect and hemianopia (Walker 1991, Doricchi 2002). Two hemispherectomy outcome studies included results from bisection tasks. Left hemispherectomised case MP (Marriotti 1998) and left hemispherectomised cases KOF and JSY (Ogden 1989) were unimpaired on line bisection tasks, though it is not clear if these tasks consisted of single trials, and no information regarding scoring criteria were given. More recently, Hausmann et al (2003) concluded that multi trial line bisections of four hemispherectomised patients demonstrated contralesional bias as a result of hemianopia. Further study is needed to confirm this finding in a larger group of patients and to see if other bisection patterns are evident such as symmetrical or pseudoneglect, or centripetal biases. There is also insufficient evidence to determine whether hemisphere specific differences exist. Regarding visual search, 4 studies report intact target detection in hemispherectomy patients (Ogden 1989, Sergent 1989, Marriotti 1998, Chiricozzi 2005). Cases KOF and JSY demonstrated mild inattention to letters in the periphery of the right hand side of the display, which is common in patients with hemianopia (Walker 1991). With the exception of the right hemispherectomised patient reported by Chiricozzi (2005), these hemispherectomy outcome studies involved simple line cancellation tasks, and none of the studies used more than one type of search task to explore the effects of target:distractor ratios. The capacity of the isolated left and right hemisphere to subserve attentional tasks that involve different target:distractor ratios remains to be elucidated.

4.1.8 Further considerations

It is possible that patients with hemianopia also have neglect, but there are few attempts to uncouple retinotopic from egocentric frames of reference to confirm the existence of pure hemispatial neglect (Bisiach 1985, Rapcsak 1987, Karnath 1991). Though at each fixation, patients with post chiasmal lesions are unable to see part or all of the contralateral visual field, they are still able to conduct a visual search across the entire visual field as evidenced in performance on cancellation tasks (Walker 1991). Indeed, the search path demonstrates evidence of exploratory saccades into the blind hemifield (Pambakian 2000, Behrmann 1997, Zihl 1995). This suggests that when attention is essentially intact, hemianopic patients can generate an occulomotor strategy that can circumvent the effects of visual field impairment to enable a complete target search of the entire visual field, even though each fixation provides an incomplete view (Zangmeister 1995). On the contrary, line bisection tasks are confounded in hemianopic patients according to some authors. Early reports of hemianopic patients showing a contralesional displacement in line bisection tasks (Axenfeld 1894, Liepmann 1900) have been confirmed by later studies (Kerkhoff 1993, Barton and Black 1998). Exceptions do exist however (Ferber 2001). Barton suggests that hemianopic patients utilise their awareness of a field defect to create a gradient of attention that is greatest for the hemianopic field, with concomitant biases in line bisection. An adaptive alteration in spatial attention may therefore preclude the possibility of pathological alteration of spatial attention in hemianopia, thus separating it from neglect. This is tenuous however, as patients with hemianopia may still demonstrate neglect, as evidenced by tasks that separate the effects of visual field impairment and visual attentional difficulties (Wilson 1987, Walker 1991).

Generic effects of cognitive impairment may also influence performance on measures of attention, with impaired performance on selective and sustained attention tasks reported in both adults (Stella 2003) and children (Swanson 1983, Perrine 1999, Sanchez-Carpintero and Neville 2003) with global cognitive impairment. As attention is always measured indirectly via performance on a particular task, demands placed on memory, reasoning, comprehension and motor speed inevitably result in lower scores when one or more of these factors are below the average range and are necessary to complete the task effectively.

4.2 Aims and predictions

It is beyond the scope of this thesis to examine each aspect of visual attention in detail. The current study is therefore focused on spatial attention in relation to visual hemineglect, and the integrity of selective attention in relation to visual search for targets amongst distractors. The principal aims of this neuropsychological study of visual attention were therefore (1) to characterize the nature and extent of any impairment in spatial attention and visual search in patients and controls; (2) to determine the relationship between side of hemispheric injury and task performance; (3) to determine whether spatial attention and visual search are more efficient when mediated by two functional cerebral hemispheres; (4) to address the issue of age at onset of seizures on task performance.

Between groups comparisons of neuropsychological data from the patient and control groups were carried out. The predictions were as follows:

- The left and right hemispherectomy groups will not demonstrate symptoms of neglect, as recovery periods will have decreased the probability of detecting it and the remaining hemisphere is not inhibited by its damaged counterpart.
- Hemispherectomy patients will demonstrate a contralesional bias in line bisection tasks.
- Centrally placed lines in line bisection tasks would be less susceptible to pathological deviations in patient and control groups, due to absence of spatial positioning bias.
- Patients will perform more poorly than controls on complex search tasks as a function of loss of division of labour between the hemispheres. This will be most evident in the right hemispherectomy group due to loss of the hemisphere that appears to be dominant in vigilant search and feature binding.
- Age at seizure onset will be positively correlated with task performance in left hemispherectomy patients as a function of decreasing plasticity and subsequent resistance to crowding effects.

4.3 Methods

4.3.1 Spatial attention in relation to visual hemineglect

The Line bisection subtest of the Behavioural Inattention Test battery (BIT) (Wilson, Cockburn and Halligan 1987) was administered to provide a simple measure of spatial attention. The test is commonly used as a screen for visual hemineglect, and consists of three horizontal lines 20.8cm in length on a landscape oriented A4 page. The centre of line one is displaced to the left of the midline, line two is placed centrally, and the centre of line three is displaced to the right. The test is more reliable than classic single trial versions of line bisection tasks (Schenkenberg

1980, Lezak 1995). Subjects are required to draw a pencil mark in the centre of each line. Deviations greater than 13mm from the midline are regarded as pathological. The manual of the BIT provided a simple scoring system that took into account performance on all three lines. Deviations between 0-12.75 mm were given 3 points, deviations between 12.76-13.75mm were given 2 points and deviations between 13.76-14.75 were given 1 point. The score for each line was summed to produce a possible maximum of 9 points. Scores below 7 were regarded as pathological. It is acknowledged that these scores are based on adult performance, though previous literature suggests the vast majority of children aged above 6 years are able to bisect within a 10mm error margin (Dellatolas 1996).

Line bisection is one of several possible methods used to screen for visual hemineglect, and dissociations between performances in different measures of neglect have recently been observed. Ferro and Kertesz (1984) reported a patient with intact performance on a cancellation task, but with marked rightward deviations evident in line bisection. Other studies provide evidence for double dissociation, with some patients being impaired on cancellation tasks but not line bisection, and vice versa (Marshall and Halligan 1995, Ferber and Karnath 2001). Overall, cancellation tasks appear to be more sensitive to neglect, perhaps due to increasing demands on visual selective attention (Rapcsak 1989).

4.3.2 Spatial and selective attention in visual search

4.3.2.1 Star cancellation

The Star Cancellation test from the Behavioural Inattention Test (BIT) was administered to provide a simple measure of both spatial and selective visual attention. Subjects were presented with a landscape oriented A4 page containing a random array of 52 large and 54 small stars, 13 letters and 10 short words (distractor: target ratio 1.39:1). Subjects were required to cancel (cross out) each of the 54 small stars within the array, scoring one point for each target correctly cancelled.

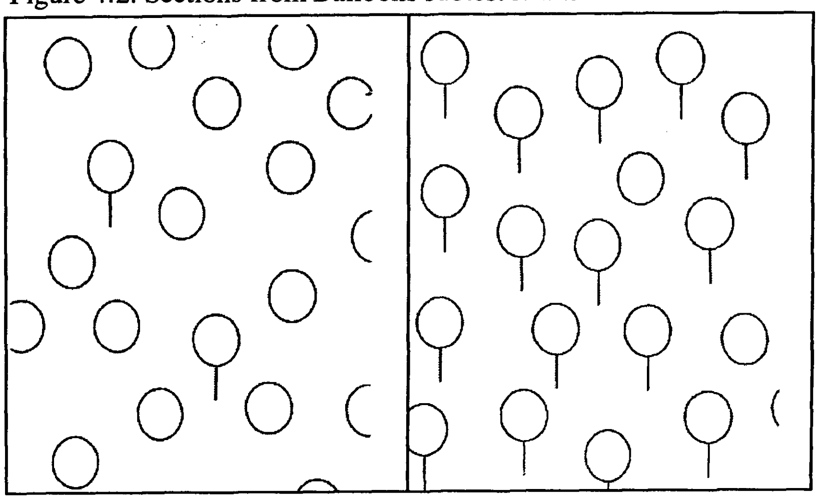
Figure 4:1. Section of the star cancellation test (Lezak 1995)

Cancellation tasks containing targets and distractors superseded traditional tests of visual neglect such as Albert's line crossing task (Albert 1973), which involved simple target detection without distractors. Impairments on this task are associated mostly with right hemisphere lesions, which manifest as failure to cancel targets on the left side of the array (Halligan 1992). The cut off level for adults on this task is 51 targets. As the star cancellation task is a relatively simple cancellation task due to targets and distractors being easily discriminated, further cancellation tasks were administered to test the limits of visual search efficacy in patients and controls.

4.3.2.2 *The Balloons test*

The Balloons test (Edgeworth, Robertson and McMillan 1998) was administered to provide a measure of spatial and selective visual attention within an A3 array. This is a screening test for visual neglect following brain injury, and attempts to separate attentional problems from visual field impairments. The test is particularly sensitive to right hemisphere damage. The test consists of two A3 landscape oriented stimulus sheets containing a random array of circles and balloons. In subtest A, 22 target balloons are interspersed between 180 circles. Ten targets and 90 distractors are placed either side of the midline (distractor: target ratio 9:1), with two extra targets close to the midline used to demonstrate the task. Subjects are given three minutes to cross out as many balloons as they can find, scoring one point for each target correctly cancelled. In subtest B, the number and position of the balloons and circles is exactly the reverse of subtest A. thus, 90 balloons and 10 circles are presented on either side of the midline, again with two central circles to demonstrate the task. The three minute time limit also applies to subtest B. Subtest A requires parallel search between targets and distractors due to the "pop out" nature of the targets (Treisman and Gelade 1980), whereas subtest B requires serial search as the "pop out" phenomena is absent.

Figure 4:2. Sections from Balloons subtest A and Balloons subtest B

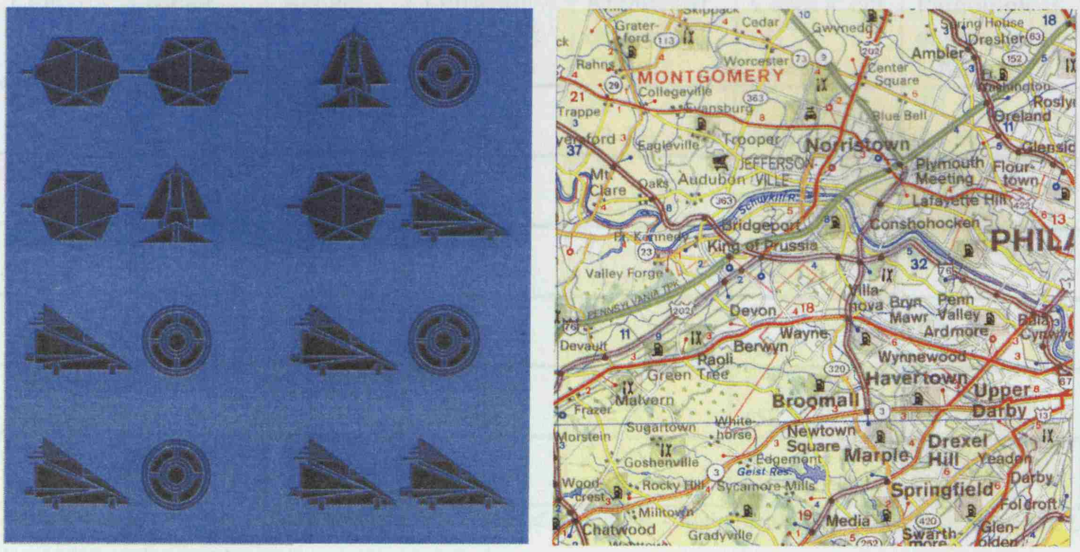


Subtest B therefore places greater demands on attentional resources than subtest A, and discrepancies between scores in the two subtests enable partitioning of the effects of hemianopia and inattention. Low scores due to visual field impairments would affect both scores equally, whereas attentional problems would differentially affect subtest B due to increased demands on attentional resources to complete this task. The cut off level for adults on version B is 17 targets.

4.3.2.3 Sky search and Map mission tests

The Sky Search and Map Mission subtests of the Test of Everyday Attention in Children (TEA-ch) (Manly et al 1999) were administered to provide a measure of spatial and selective visual attention that enables separation of perceptual and motor components of the task. These tests also differ from the star cancellation and balloons tests as target stimuli in the Map Mission subtest are much smaller and more numerous, and stimuli in the Sky Search task are arranged in columns rather than random arrays, thus encouraging a systematic search process. The Sky Search test is composed of two parts. Part one consists of an A3 landscape oriented stimulus sheet containing 10 columns of stimuli. Stimuli were composed of pairs of spaceships that were either identical or different. Subjects were required to cross out all pairs that had identical members as quickly as possible. There were 20 targets in total, distributed amongst 108 distractors (distractor: target ratio 5.4:1). Subjects scored 1 point for each pair correctly cancelled, producing a total of 20 points. Part 2 of the Sky Search test gives a measure of ability to select targets without distractors, enabling calculation of actual cancellation speed. The test consisted of an A3 landscape oriented stimulus sheet with the 20 identical spaceship pairs in their original positions, but without distractors. Subjects were required to cross out all targets as quickly as possible, again scoring 1 point for each pair correctly cancelled.

Figure 4:3. Sections from Sky Search and Map Mission tests (Manly et al 1999)



The map mission test consists of an A3 landscape oriented stimulus sheet containing a random array of black symbols (4 x 3 mm) superimposed on a roadmap type background. There are 80 small targets (Knife and fork symbols in version A and petrol pumps in version B) amongst 92 distractor symbols (distractor: target ratio 1.15:1). Subjects were given one minute to cross out as many target symbols as possible, scoring one point for each symbol correctly cancelled. All study participants were given version B of this test.

4.4 Analyses

Analyses of neuropsychological data were carried out as described in chapter 2. ANOVA design, factors and covariates will be referred to throughout the results section as appropriate. Medians replace means where variables did not follow a normal distribution.

4.5 Results

4.5.1 Line Bisection

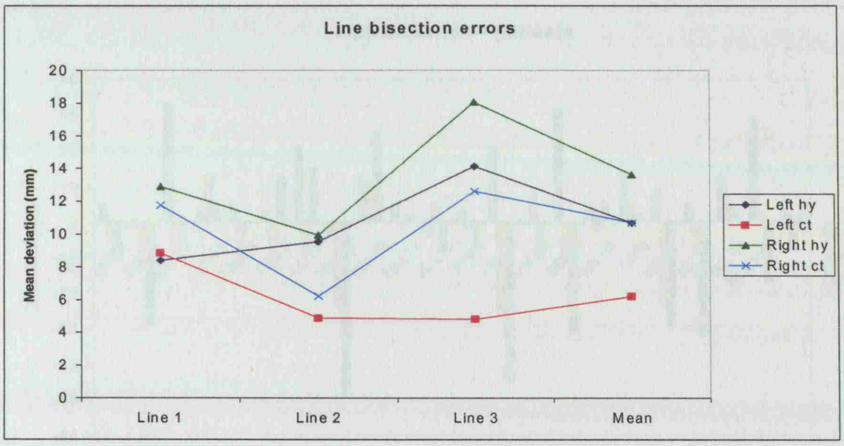
Table 4.1 and figure 4.4 summarise results for the patient and control group. Repeated measures ANCOVA (using age at test and PIQ as covariates) was used to test for differences between left and right hemispherectomised patients, and also for differences between patients and controls. It was also of interest to see whether spatial positioning of lines would affect performance. Within subjects factor *Line* (3 levels pertaining to scores for line 1, 2 and 3) and between subjects factors of hemisphere (left, right) and group (patient, control) were included. There was no evidence for an interaction between any of the variables. There was also no evidence of main effects.

Table 4.1. Line bisection deviations in mm for patient and control group.

Line	Mean (+/-SEM)	Range	Leftward deviations (Range)	Rightward deviations (Range)	Cases < cut off (Hand)	Pathological deviations to left/right
Line 1 Patients	10.43 (2.17)	1-33	4 (1-4)	18 (2-33)	7 (4R, 3L)	7R
Line 1 Controls	10.08 (2.07)	1-29	4 (1-5)	15 (1-29)	7 (3L, 4R)	7R
Line 2 Patients	9.73 (1.52)	1-25	15 (1-25)	7 (2-13)	6 (3L, 3R)	5L, 1R
Line 2 Controls	5.42 (2.33)	0.5-22.5	11 (0.5-12)	8 (1-22.5)	2 (2R)	2R
Line 3 Patients	15.91 (3.11)	0.5-48	13 (0.5-48)	9 (2-25)	9 (5R, 4L)	7L, 2R
Line 3 Controls	8.77 (2.35)	1-39	17 (1.5-39)	2 (1-5)	3 (3R)	3R

(Note that L and R cases indicate handedness and side of surgery (R – Right hemispherectomy, right handed, L-Left hemispherectomy, Left handed).

Figure 4:4. Magnitude of Line bisection errors for patients and controls.



Nine patients (4 left and 5 right hemispherectomy) were below the cut off level of the task, 2 of which were below 17 years of age. In contrast, only 3 controls were below the cut off level, 2 of which were aged below 17 years. Statistical analysis using Fishers exact tests revealed a trend towards differences in the proportion of patients and controls that were below or at/above the cut off scores for this task, but this did not reach statistical significance ($p = .077$). The observed pattern of bisection methods for lines displaced from the midline is presented in table 4.2 and figures 4.5 and 4.6. Bisections towards the active hand were made consistently in 7 patients and 3 controls, with bisections being made in the opposite direction in 6 patients and 4 controls. As the active hand also correlates with the intact visual field in patients, it seemed that approximately equal numbers of patients made bisections that deviated towards or away from the hemianopic field, with no marked differences in the number of left and right hemispherectomy cases in each category, which did not confirm the prediction regarding contralesional bias. Cases **PO$_L$2** and **LO$_L$8** were below the cut off level for this task and bisected lines towards the active hand, which may be interpreted as an effect of hemianopia or neglect. 2 right handed controls consistently bisected lines to the left, thus demonstrating pseudoneglect. A bisection pattern commonly observed was the tendency of bisecting left lines rightwards and vice versa, reflecting a centripetal bias. This was observed in over a third of patients and more than half of the control group. Mean bisection errors incorporating direction of bias are illustrated in figure 4.7, and suggest a general tendency towards centripetal bias in all groups for lines 1 and 3.

Table 4.2. Bisection methods observed in patients and controls

	Towards active hand	Away from active hand	Centripetal
Patients > cut off	5	5	3
Controls > cut off	3	4	9
Patients < cut off	2	1	6
Controls < cut off	0	0	3

Figure 4:5. Bisection profiles for each line – patient group

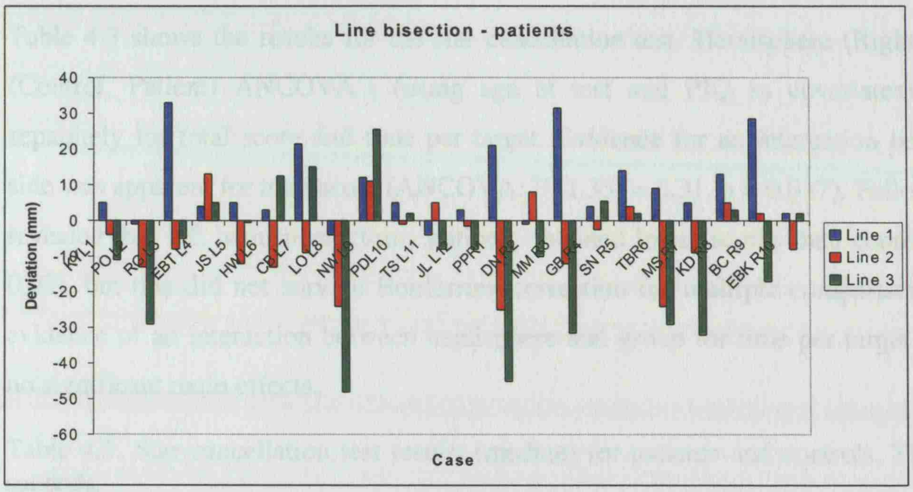


Figure 4:6. Bisection profiles for each line – control group.

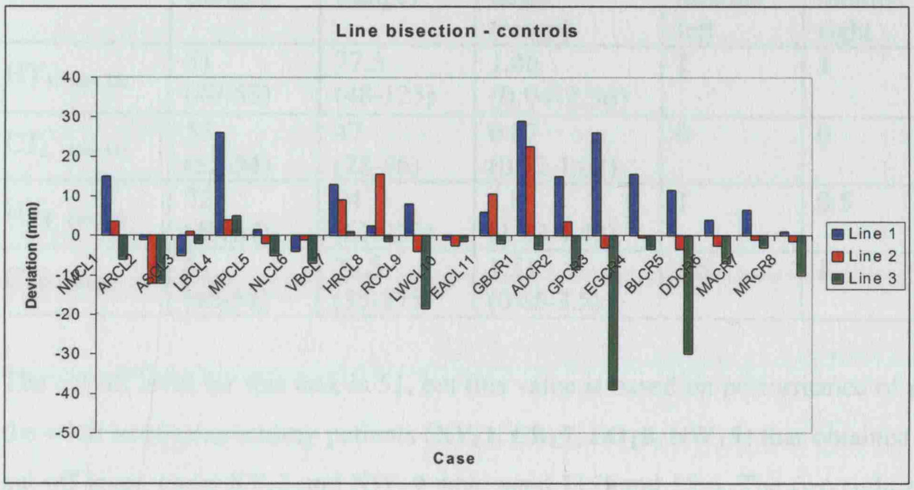
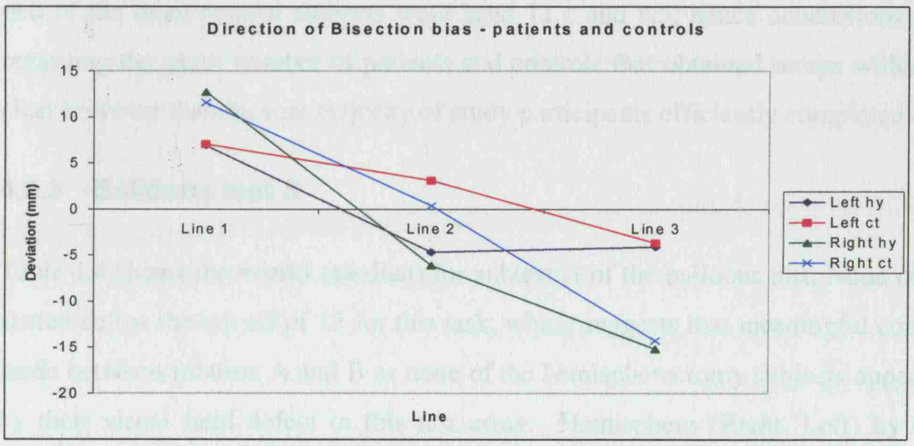


Figure 4:7. Direction* of Line Bisection errors for patients and controls.



*Negative values indicate leftward bias, positive values indicate rightward bias.

4.5.2 Star Cancellation

Table 4.3 shows the results for the star cancellation test. Hemisphere (Right, Left) by Group (Control, Patient) ANCOVA's (using age at test and PIQ as covariates) were computed separately for total score and time per target. Evidence for an interaction between group and side was apparent for total score (ANCOVA: $F(1,35) = 6.31$, $p = 0.017$). Follow up using t tests revealed that left hemispherectomy patients obtained lower scores than controls ($t = 3.85$, $p = 0.02$), but this did not survive Bonferroni correction for multiple comparisons. There was no evidence of an interaction between hemisphere and group for time per target. There were also no significant main effects.

Table 4.3. Star cancellation test results (median) for patients and controls. Times are given in seconds.

Group	Score (range)	Time (range)	Time per target (range)	Total omitted left	Total omitted right	Total omitted
HY_L (N= 12)	51 (48-53)	77.5 (48-123)	1.46 (0.94-2.56)	1	1	3
CT_L (N= 11)	53 (52-54)	47 (28-86)	0.87 (0.52-1.62)	0	0	0
HY_R (N= 10)	52 (48-54)	94 (61-230)	1.9 (1.13-4.42)	1	0.5	2
CT_R (N= 8)	51 (45-54)	79.5 (35-175)	1.51 (0.65-3.5)	1.5	1	2.5

The cut off level for this task is 51, but this value is based on performance of adult subjects. Of the 4 left hemispherectomy patients (**KY_L1, CB_L7, LO_L8, NW_L9**) that obtained scores below the cut off level, cases **KY_L1** and **NW_L9** were aged 11:3 and 15:6. The two right hemispherectomy patients (**DN_R2, MM_R3**) that obtained scores below the cut off level were aged 8:0 and 11.5, and two of the three control subjects were aged 11.1 and 8.5, hence conclusions cannot be drawn regarding the small number of patients and controls that obtained scores within this range. It is clear however that the vast majority of study participants efficiently completed this task.

4.5.3 Balloons test A

Table 4.4 shows the results (median) for subtest A of the balloons test. None of the participants scored below the cut off of 17 for this task, which suggests that meaningful comparisons can be made between subtests A and B as none of the hemispherectomy subjects appear to be hindered by their visual field defect in this test array. Hemisphere (Right, Left) by Group (Control, Patient) ANCOVA's (using age at test and PIQ as covariates) were computed separately for total score and time per target. Statistical analyses revealed no evidence of an interaction between hemisphere and group for total score or time per target on this task. It was therefore appropriate to look at main effects. Evidence for a main effect of group was observed for total score on the Balloons A test (ANCOVA $F_{1, 35} = 4.13$, $p = 0.05$), with patients obtaining lower scores than controls.

Table 4.4. Balloons test A – patients and controls

Group	Score (range)	Time (range)	Time per target (range)	Total omitted left	Total omitted right	Total
HY_L (N= 12)	19 (17-20)	51 (29-127)	2.7 (1.61-6.35)	0	0	1
CT_L (N= 11)	20 (20)	28 (15-65)	1.4 (0.75-3.25)	0	0	0
HY_R (N= 10)	20 (18-20)	67 (30-96)	3.35 (1.5-5.05)	0	0	0
CT_R (N= 8)	20 (17-20)	50 (28-103)	2.5 (1.40-6.06)	0	0	0

4.5.4 Balloons test B

Table 4.5 shows the results (median) for subtest B of the balloons test. Hemisphere (Right, Left) by Group (Control, Patient) ANCOVA's (using age at test and PIQ as covariates) were computed separately for total score and time per target. Statistical analyses showed no evidence of an interaction between group and side for any of the variables listed. It was therefore appropriate to look at main effects.

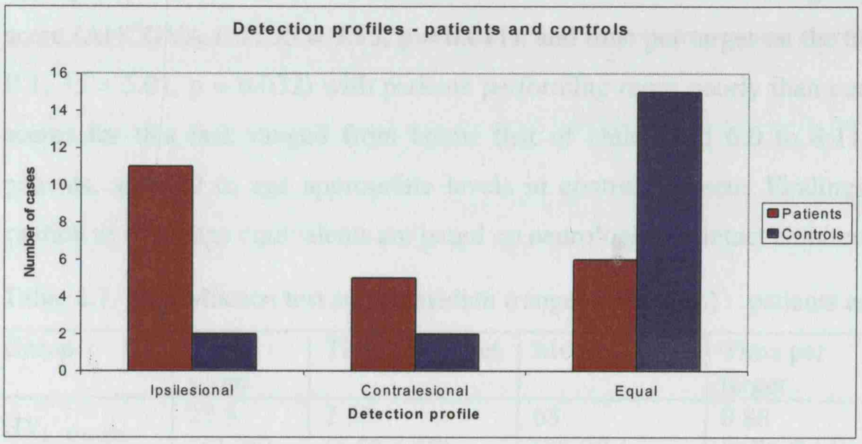
Table 4.5. Balloons subtest B – patients and controls.

Group	Score (range)	Time (range)	Time per target (range)	Total omitted left	Total omitted right	Total
HY_L (N= 12)	14 (3-18)	133.5 (30-180)	10 (4.38-22.50)	3	4.5	7.5
CT_L (N= 11)	17 (9-20)	120 (79-180)	7.17 (4.83-13)	1	2	3
HY_R (N= 10)	13.5 (4-17)	180 (96-180)	13.2 (10.59-45)	3.5	4.5	6.5
CT_R (N= 8)	16.5 (10-20)	155 (94-180)	9.5 (4.7-18)	1.5	1	3.5

Evidence for a main effect of group was found for total score (ANCOVA $F_{1, 35} = 14.416$, $p = 0.001$) and time per target (ANCOVA $F_{1, 35} = 4.32$, $p = 0.45$), with patients performing more poorly than controls. Repeated measures ANCOVA (using age at test and PIQ as covariates) was computed to examine differences in scores for serial and parallel search. The balloons task provided the most appropriate opportunity to test this prediction as the simple and complex versions of the task employ the same stimuli. Within subjects factor of *test* (2 levels pertaining to scores for subtests A and B) and between subjects factors of hemisphere (left, right) and group (patient, control) were included. Scores obtained in subtest A were significantly higher than scores obtained in subtest B across groups (ANCOVA $F_{1, 35} = 36.76$, $p < 0.001$).

The cut off level for subtest B of the balloons task is 17, which is based on adult performance levels and so results are interpreted with caution. 6 of 7 (86%) adult left hemispherectomy patients, 2 of 6 (33%) adult left control subjects, 6 of 7 (86%) adult right hemispherectomy patients and 1 of 5 (20%) adult right control subjects obtained scores that were below this level. Statistical analyses using Fishers exact test revealed significant differences between the number of adult patients and controls above and below the cut off level for this task (p =. 005), with patients performing more poorly than controls. Target detection profiles for balloons subtest B were examined with respect to percentage of targets missed within ipsi and contralesional space (ipsi and contralateral to active hand in controls). Total targets detected on the left and right halves of the array were used to calculate a ratio between number of targets cancelled on each side versus total targets cancelled. A ratio between 45-55 percent was interpreted as similar numbers of targets cancelled on both sides of the array. Ratios outside this parameter were interpreted as an ipsi or contralesional bias, depending on which half of the array contained most detected targets. These details are summarised in Figure 4.8. Chi square test revealed significant differences in proportion of patients and controls demonstrating each cancellation pattern ($x^2 = 11.214$, p = 0.01).

Figure 4:8. Detection profiles for Balloons subtest B – patients and controls



4.5.5 Sky Search

Table 4.6 shows the results (median) for the sky search test. Hemisphere (Right, Left) by Group (Control, Patient) ANCOVA's (using age at test and PIQ as covariates) were computed separately for total score and time per target for the task proper and its motor control subtest. There were no interactions or effects. Attention scores for the left hemispherectomy group range from below the mean expected for a child aged 6:0 to an age equivalent of 15:0. Similar lower limits were found for all groups. Upper limits for the left control group, right hemispherectomy group and right control group were 11:0, 13:0 and 16:0 respectively. Findings are interpreted with caution as these age equivalents are based on neurologically intact children.

Table 4.6. Sky search test scores - median (range in brackets) : patients and controls

Group	Total	Total time	Time per target	Motor score	Motor time	Time per target	Attention
HY_L (N= 12)	14.5 (4-20)	128 (73.4-264)	8.63 (3.67-66)	18 (17-20)	17 (11.85-46)	0.97 (0.66-2.56)	7.79 (2.84-64.61)
CT_L (N= 11)	18 (10-20)	120 (63-210)	6.67 (4.85-11.75)	19 (18-20)	17 (7-26)	0.89 (0.39-1.44)	5.8 (4.2-11.3)
HY_R (N= 10)	14 (6-20)	132 (72-239)	11.9 (3.6-30.3)	19.5 (17-20)	21 (13-42)	1.08 (0.65-2.18)	10.31 (3.0-28.5)
CT_R (N= 8)	14 (7-20)	128 (58-292)	9.09 (2.9-41.7)	19.5 (18-20)	20.5 (13-60)	1.14 (0.65-3.33)	8.1 (2.3-38.4)

4.5.6 Map Mission

Table 4.7 shows the results (median) for the map mission test. Hemisphere (Right, Left) by Group (Control, Patient) ANCOVA's were computed separately for total score and time per target for the task proper and its motor control subtest. Statistical analyses showed no evidence of an interaction between group and side for any of the variables listed. It was therefore appropriate to look at main effects. Evidence for a main effect of group was found for total score (ANCOVA F 1, 35 = 7.15, $p = 0.011$), and time per target on the task proper (ANCOVA F 1, 35 = 5.01, $p = 0.032$) with patients performing more poorly than controls. Age equivalent scores for this task ranged from below that of child aged 6:0 to 8:11 in hemispherectomy patients, and 6:0 to age appropriate levels in control subjects. Findings are interpreted with caution as these age equivalents are based on neurologically intact children.

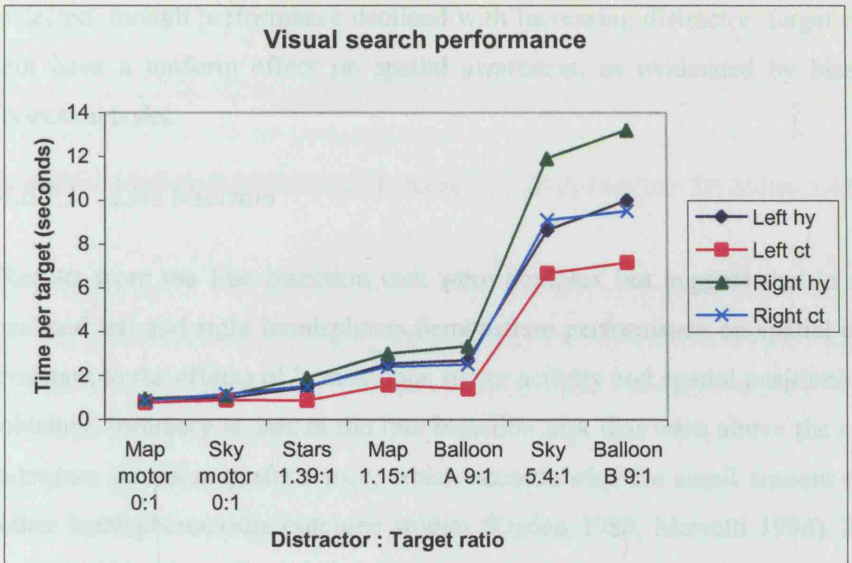
Table 4.7. Map Mission test scores median (range in brackets) : patients and controls

Group	Total score	Time per target	Motor score	Time per target	Attention
HY_L (N= 12)	23.5 (13-38)	2.55 (1.58-4.62)	68 (28-80)	0.88 (0.75-2.14)	1.35 (0.47-3.28)
CT_L (N= 11)	38 (21-54)	1.57 (1.11-2.86)	78 (46-80)	0.77 (0.75-1.3)	0.8 (0.36-1.7)
HY_R (N= 10)	20 (9-33)	3 (1.82-6.67)	63 (44-80)	0.95 (0.75-1.36)	2.05 (1.07-5.73)
CT_R (N= 8)	25 (18-46)	2.40 (1.3-3.33)	70.5 (34-80)	0.85 (0.75-1.76)	1.37 (0.55-1.73)

4.5.7 Distractor: target ratios and time per target scores

Figure 4.9 shows the relationship between distractor: target ratios and mean time per target scores on each of the search tasks administered in this study. It is of note that distractor target ratios below 2:1 result in relatively fast time per target scores. Ratios above 5:1 result in marked increase in time per target scores when the target is similar to or less conspicuous than distractors, with the exception of subtest A of the Balloons task. The low time per target ratio for subtest A of the Balloons test reflects the parallel nature of the search as targets are more conspicuous than distractors, and thus the high distractor: target ratio is advantageous. The profiles are similar across groups.

Figure 4:9. Visual search performance – patients and controls.



4.5.8 Age at clinical onset of pathology and seizure onset

Correlational analyses were run between age at onset of seizures and results of each of the assessments reported above. Partial correlations were run to control for age at test where appropriate. For the left hemispherectomy group, age at seizure onset was positively correlated with total score on the Balloons B task (R = 0.592, p = 0.055), but it was just outside statistical significance. For the left control group, age at seizure onset was positively correlated with total score on the Balloons B task (R = 0.819, p =0.046), and total score on the Sky Search Motor control subtest (R = .913, p = 0.011). There were no significant correlations for the right hemispherectomy group. For the right control group, positive correlations were found between age at seizure onset and total scores on Sky Search task proper (R = 0.875, p = 0.01).

4.6 Discussion

The principal aims of this neuropsychological study of visual attention in hemispherectomised patients were to characterize the nature and extent of any impairment in this domain, to determine the relationship between side of hemispheric injury and task performance, and to determine whether visual attention was more efficient when mediated by two functional cerebral hemispheres. It was also important to determine if there was a relationship between age at seizure onset and integrity of visual attention.

4.6.1 The integrity of spatial and selective attention

Overall, the results of the various assessments reported in this chapter provided convergent evidence that the isolated left and right hemispheres possess a basic working model of visual attentional function and were able to direct attention to explore both sides of space. Attentional focus was narrowed according to goal directed objectives and sustained until targets were selected, though performance declined with increasing distractor: target ratios. Hemianopia did not have a uniform effect on spatial awareness, as evidenced by bisection profiles in line bisection tasks.

4.6.1.1 Line bisection

Results from the line bisection task were complex but suggest that in a subset of cases, the isolated left and right hemispheres demonstrate performance on spatial awareness tasks that is resistant to the effects of hemianopia, motor activity and spatial positioning of lines. 13 patients obtained summary scores in the line bisection task that were above the cut off level, reflecting adequate bisection performance, which accords with the small amount of data available from other hemispherectomy outcome studies (Ogden 1989, Mariotti 1998). Results from bisection errors of line 2 confirmed that 4 patients (**KY$_{L}$1, TS$_{L}$11, SN$_{R}$5, KD$_{R}$8**) and 6 controls were capable of making bisections of centrally presented lines within 3-5mm, thus approximating performances of children aged 7:6 years. Bisections within 2mm as seen in the adult population and children aged above 11:0 were observed in 4 patients (**PD$_{L}$10, JL$_{L}$12, GB$_{R}$4, BC$_{R}$9**) and 8 controls aged 13:0 and above, suggesting age appropriate levels of performance. It is acknowledged that performance was highly variable in each group, with a subset of patients and controls demonstrating impaired performance on this task. This suggests that global reduction in cognitive function may contribute to impaired performance on this task, and a variety of pathological bisection errors become apparent.

The classic finding in neglect is that of consistent ipsilesional displacements during line bisection, a phenomenon that was observed in only two right hemispherectomy patients in this study (**SN$_{R}$5, KD$_{R}$8**), both of whom were above the cut off level of the task. There were also 5 cases demonstrating ipsilesional displacements in the left hemispherectomy group including two subjects (**PO$_{L}$2, LO$_{L}$8**) that were below the cut off level. Presence of right hemineglect in these two cases was rendered highly unlikely when one considers performance on visual search tasks and drawing tasks (see chapter 7), though it is acknowledged that neglect can be fractionated into task specific syndromes (Halligan and Marshall 1992, Ferber and Karnath 2001). Ipsilesional biases in hemispherectomy cases may in fact reflect failure to decouple attention from motor activity, with bisections being placed towards the active hand, thus resembling symmetrical neglect type bisection patterns seen in young children (Bradshaw 1988, Dellatolas 1996, Dobler 2001). Symmetrical neglect is attributed to callosal immaturity rendering spatial representation vulnerable to current motor activity, which accords with lack of callosal transfer in these patients. Ipsilesional biases in both left and right hemispherectomised patients suggests that both hemispheres may be influenced by motor activity in the absence of bilateral hemispheric input, which argues against the assumption that only the left hemisphere is influenced by motor activity in the absence of right hemispheric input (Heilman 1984, Kashiwagi 1990, Corballis 1995). It remains to be seen however, why a similar proportion of patients demonstrate the opposite tendency to bisect lines away from the active hand, which is more suggestive of compensatory biases

Whilst contralesional bisection biases were present in a subset of patients, findings in this study are at odds with studies that suggest all hemianopic patients consistently demonstrate a contralesional displacement in line bisection tasks (Behrmann et al 1997, Barton and Black 1998, Dorrichi et al 2002). A recent study of 4 hemispherectomy patients claims that the same phenomenon exists in these patients (Hausmann 2003), though the study sample is extremely small and so it remains possible that results obtained represent a fraction of possible bisection strategies in hemispherectomised patients. Barton (1998) suggests that hemianopic patients utilise their awareness of a field defect to create a gradient of attention that is greatest for the hemianopic field. Space within the hemianopic field acquires greater salience and as such, eliminates neglect and manifests as contralesional bisection bias. Whilst the findings in Barton's study may only apply to a small proportion of study participants demonstrating relevant bisection biases, the suggestion of an adaptive alteration in spatial attention makes intuitive sense when considering the lack of neglect demonstrated by hemispherectomy patients in this study, and may have some relevance when considering performance on search tasks. It is also acknowledged that task differences may play a part in discrepant results. Contralesional bisection biases reported in previous studies (Barton and Black 1998, Hausmann 2003) are averaged over 10-20 lines, whereas the current study used only three lines. It is possible that using more trials would have yielded a mean bisection error towards the contralateral field, but it cannot be ignored that some patients consistently bisected towards the intact hemifield.

Centripetal biases were also observed in patients and controls. Overall, both patients and controls tended towards rightward deviations when bisecting line 1, and leftward deviations when bisecting line 3, which supports the notion of a relationship between spatial positioning of lines and deviation of bisection towards the body midline (Nichelli 1989, Nielsen 1999). Whilst strategies appeared to be evenly distributed in hemispherectomised patients above the cut off level of the task (see table 4.2), the majority of control subjects with scores above the cut off level demonstrated a centripetal bias. Almost all patients and controls whose scores were below the cut off level demonstrated this type of bias, suggesting that the presence of the centrally placed line may have adversely affected performance in some individuals by creating pathological bisection biases in left and right lines towards the centrally placed line. It is acknowledged however that overall, there were no significant differences in the magnitude of bisection errors between the centrally placed and peripherally situated lines.

A second, concurrent possibility is that some participants are susceptible to the over representation of the central portion of the visual field, producing the centripetal bias. This is plausible, as the central field is disproportionately represented at almost all levels of the visual system, from the retina (Rovamo 1979) to striate and extrastriate areas (Van Essen 1984, Maguire 1984). Whilst this may contribute to accounting for the observed prevalence of centripetal bisection errors, it is clear that a variety of bisection patterns exist, and competing accounts of line bisection performance such as ipsi/contralesional biases, symmetrical neglect and centripetal tendencies may in fact represent the spectrum of possible strategies available and the sources of such biases such as motor activity, hemianopia and spatial positioning of lines.

In summary, it seems that the isolated left and right hemispheres were able to consider left and right sides of space in relation to the midpoint of line stimuli, though spatial positioning of lines, hemianopia and use of active hand may have affected performance in some individuals, whilst others were able to bisect accurately in the presence of these three factors. A variety of bisection strategies were present that support the phenomena of symmetrical neglect (Bradshaw 1988), bisecting towards the contralesional field (Barton and Black 1998, Hausmann 2003), and centripetal biases (Nielsen 1999), suggesting that these models of bisection strategies may each contribute towards an explanation of task performance in heterogenous groups.

4.6.1.2 Visual search

Results from the visual search tasks demonstrate that both patients and controls can effectively employ selective attention to mediate goal directed objectives on visual search tasks when the attentional demands are relatively low, as indexed by distractor: target ratio and the size of the array. This implies that the basic framework of attentional function as outlined by Treisman (1980, 1998) and Posner and Petersen (1990) is intact within the isolated left or right hemisphere, as attentional focus was effectively shifted around the search field, narrowed according to goal directed objectives, and sustained until targets were correctly selected.

Evidence of effective parallel and serial search within simple arrays comes from scores obtained on subtest A of the Balloons test and the stars test respectively. Scores on the stars task ranged from 83-96 percent in terms of detection rate, with most participants detecting targets every 0.5-3 seconds. The targets on the stars task were relatively distinct from distractors, though the presence of larger stars does require conjunction of size and shape in addition to simple target detection. The Balloons task is another example of a visual search task requiring detection of a single target type within a random array, but the search is conducted over an A3 array, and the distractor: target ratio is much higher. Nevertheless, subtest A permitted rapid, efficient detection via parallel search, due to the small number of salient targets defined by a single feature, that were hidden amongst more numerous but less conspicuous distractors. Between 85-100 percent of targets were detected by all groups, with most participants detecting targets every 1-5 seconds. Additionally, all participants scored above the cut off for this task, suggesting that hemianopia did not pose problems for the hemispherectomy patients when searching an A3 array. This accords with previous studies suggesting hemianopic patients can effectively explore the contralesional hemifield (Pambakian 2000, Behrmann 1997, Zihl 1995). Results from the star cancellation test and subtest A of the balloons test did not reveal any differences between left and right hemispherectomy patients, and no instances of hemineglect, which suggests the isolated left and right hemisphere demonstrate similar levels of performance on visual search tasks that contain salient targets within a random array. These results lend weight to findings from left (Ogden 1989, Marriotti 1998) and right (Sergent and Villemure 1989, Chiricozzi 2005) hemispherectomy case studies that demonstrate intact visual search.
Subtest B of the Balloons task provided a measure of conjunction search in the context of a relatively large distractor target ratio where distractors are more salient than targets. All groups obtained lower scores on subtest B of the Balloons task, with detection rates between 50-100 percent for controls and a more varied 15-90 percent for patients. Most participants detected targets every 5-13 seconds in the control group, and 7-20 seconds in the patient group, somewhat slower than Balloons subtest A. Differences between performance on simple and complex tasks illustrate the difficulties of serial as opposed to parallel search as predicted by Treisman's model, and highlights limitations of attentional function in the event of generic reductions in cognitive ability. Figure 4.9 illustrated similarities between group profiles with respect to task performance and distractor: target ratios. All groups perform relatively well on tasks that have low distractor: target ratios, or particularly salient targets that encourage parallel search in the event of higher ratios, with performance declining as distractor: target ratios increase.

Comparison of performance on subtests A and B of the Balloons task eliminated the possibility of hemianopia and failure to understand test instructions as possible factors contributing to poor performance. The principal differences between subtest A and B is the nature of the search process required to detect targets. Subtest A requires relatively little attentional effort, as targets will be detected in parallel across the array due to greater salience of the additional feature (the "string"). Subtest B contains *distractors* that are of greater salience (the original target configuration in subtest A in fact). A small number of relatively weak targets are distributed amongst a much greater number of salient distractors, thus requiring a much more effortful search. The fact that all participants were able to detect at least some targets implies the discrimination process was intact, and thus selective attention was effectively narrowed in focus, and features were appropriately extracted and identified. The difficulty appeared to arise in the length of time required to detect targets, and the small number of targets detected in total which may reflect difficulties in sustaining attentional resources for sufficient periods of time required to detect stimuli, and/or failure to generate an efficient search process that would enable systematic scanning of the array and thus decrease time per target rates. Support for these assertions are found in previous studies of individuals with cognitive impairment who demonstrate decreased vigilance (Tomporowski et al 1994) and impaired visual search (Merrill et al 1996). Further support for these assertions is found upon examining individual cases in this thesis. Patients could be fractionated into several groups. Cases **KY$_{L}$1, EBT$_{L}$4, LO$_{L}$8, PD$_{L}$10** terminated the search early, yet time per target scores were better than average, suggesting difficulties sustaining attention even though the task was being completed efficiently. Cases **NW$_{L}$9, PP$_{R}$1, DN$_{R}$2, GB$_{R}$4, TB$_{R}$6,** and **BC$_{R}$9** made use of the full three minutes, but scores were below average, suggesting sustained attention and adequate target discrimination were not the only pre requisites to success on this task. Thus it seems both sustained attention and generation of a rapid, efficient search strategy were related to successful performance on subtest B of the Balloons test. Analysis of the percentage of targets cancelled on each half of the array on subtest B of the balloons task suggests that hemispherectomised patients tended to cancel targets in one half of the array within the time limit, whereas controls tended to cancel targets equally on both sides of the array. Whether this reflects slower time per target rates preventing continuation of systematic search within the time limit or a failure to detect targets in the other half of the array requires further investigation using experiments that record scanpaths and cancellation patterns in more detail.

The importance of sustained attention and search efficacy also applies to results obtained in the remaining two tasks. The map mission was another example of a search task that required detection of a single target type within an A3 array. Distractor: target ratios were much lower in this task than the Balloons task or Sky Search task, which resulted in time per target rates that were more closely akin to star cancellation and to the rapid parallel search afforded in subtest A of the Balloons test. Most participants detected target every 1.5-4.5 seconds in the patient group, and every 1-3 seconds in the control group. Detection rates varied from 11-41 percent in patients and 22.5-67 percent in controls. It becomes clear that, although time per target rates were relatively high in this task, overall detection rates were relatively low. This reflects the stringent time limit of 60 seconds for the task, hence generation of a systematic search strategy becomes paramount if one is to cancel all 80 targets within the time limit. None of the hemispherectomised patients obtained age appropriate scores on this task, and just three control participants achieved scores at this level, illustrating difficulties encountered when attempting to search an array within a stringent time limit. The sky search is another example of a search task within an A3 array. The distractor: target ratio is in between that of the Star/Map tests, and the Balloons task. The sky search is unique within the search tasks presented, as stimuli are arranged in columns, thus encouraging systematic search. Detection rates varied widely in both groups, between 20-100 percent for patients and 33-100 percent for controls. Most participants detected targets every 3-30 seconds in the control group, and 3-18.5 seconds in the patient group. There were no observed differences between groups for this task. Age equivalent scores on this task ranged from below that of a child aged 6:0 to 15:0 in both patients and controls, reflecting wide variation in attentional capacity across groups. Seven patients and ten controls obtained age appropriate scores for number of targets detected on this task, but when time per target was considered only two patients and one control participant obtained age appropriate scores.

In summary, results of the various tests of spatial and selective attention in this study are complex and indicate that a broad spectrum of performance is evident within this study group. Consideration of the pattern of performance in individual cases provides general support for group observations and also raises further interesting hints as to how these skills develop at the level of the individual child. The tests used provide various measures of spatial and selective attention that can be fractionated according to processing demands. Whilst hemispherectomised patients **KY**$_{L}$**1**, **CB** $_{L}$**7**, **LO** $_{L}$**8**, **NW** $_{L}$**9**, **MM** $_{R}$**3**, **DN** $_{R}$**2** had difficulty beyond line bisection and parallel search, others (**PO** $_{L}$**2**, **RG** $_{L}$**3**, **HW** $_{L}$**6**, **JS** $_{L}$**5**, **PP**$_{R}$**1**, **GB** $_{R}$**4**, **SN** $_{R}$**5**, **TB** $_{R}$**6**, **MS** $_{R}$**7**) also managed the simple conjunction search required in the stars test but found more difficult conjunction searches difficult. Cases **EBT** $_{L}$**4**, **PD**$_{L}$**10**, **KD** $_{R}$**8**, **BC** $_{R}$**9** were also able to take advantage of the columnar array in the sky search task, but encountered difficulties with the random array of subtest B of the Balloons test. Cases **TS**$_{L}$**11**, **JL**$_{L}$**12**, **EBK**$_{R}$**10** were successful on all of these tests, with difficulties emerging only with the stringently timed map mission test. It is of note that of the hemispherectomy patients with PIQ scores within the average range, **JL** $_{L}$**12** and **EBK** $_{R}$**10** performed very well on these tasks whereas **HW** $_{L}$**6** had difficulties beyond simple conjunction search. Both patients and controls could be grouped in a similar manner according to patterns of success and limitations, though differences between these groups do exist and are addressed in section 4.6.3.

4.6.2 Comparison of left and right hemispherectomised patients

Results from this study illustrate that the isolated left and right hemispheres are able to attain similar levels of basic attentional function, suggesting some degree of equipotentiality. This accords with neuroimaging studies illustrating bilateral hemispheric involvement in visual attention (Thiel et al 2004), studies that propose each hemisphere can independently search and discriminate within its own hemifield simultaneously (Alvarez and Cavanagh 2005, Kraft et al 2005), and results from callosotomy studies that demonstrate either hemisphere can subserve visual attention tasks (Reuter-Lorenz and Fendrich 1990, Luck 1989, Corballis 1995). Results also accord with studies of childhood cerebral injury that demonstrate similar performance regardless of side of hemispheric injury (Schatz et al 2004, Trauner 2003, Katz et al 1998). This poses problems for theories of early specialisation, though it is acknowledged that presence of brain injury may alter the course of hemispheric lateralisation of function as suggested by interactive specialisation theories. The lack of a relationship between side of hemispheric injury and task performance contrasts with literature (see section 4.1.5) claiming that the right hemisphere plays a dominant role in visual attention in both adults and children. It has been repeatedly suggested that the right hemisphere is able to direct attention to both sides of space, whereas the left hemisphere directs attention contralaterally (Heilman 1984, Mesulam 1981). According to these proposals, the right hemispherectomy group would have been subject to a greater disadvantage during line bisection and visual search tasks due to the left hemisphere neglecting the contralesional visual field, whereas left hemispherectomy patients would be able to capitalize on attentional resources that span the entire visual field. Other explanations of neglect are also incongruous with results from the current study, such as competitive inhibition models advanced by Kinsbourne (1970, 1983) and Duncan (1996). These authors suggest that neglect occurs as a result of inhibition of the damaged right hemisphere, and thus imbalance of neural activity shifts attentional focus into the intact visual hemispace. In the absence of a damaged right hemisphere, the intact left hemisphere should gain complete monopoly, yet none of the right hemispherectomised patients appear to consistently neglect the contralesional hemispace. It is possible that hemianopia may have prevented this advantage from becoming manifest, though previous work suggests that hemianopia and neglect are separable entities (Walker et al 1991, Parton et al 2004). It has also been suggested that the left hemisphere is more vulnerable to motor activity in the presence of right hemisphere damage, yet it seems that a range of line bisection strategies are observed in both left and right hemispherectomy patients, with similar levels of efficacy.

Results from search tasks accord with line bisection results and confirm that the isolated left and right hemispheres demonstrate similar levels of attentional capacity across both sides of space as target detection rates were similar in each patient group, and there were no consistent demonstrations of hemineglect which confirms the prediction in section 4.2 regarding occurrence of neglect. Results generally accord with studies of callosotomy patients in terms of absence of neglect but no right hemisphere advantage was observed in visual search tasks, hence the prediction in section 4.2 regarding functional laterality was not confirmed. It is possible that global reduction in cognitive function may prevent the expression of such advantages, but there were no marked differences between case **EBK$_R$10** and cases and **JL$_L$12**, both of whom obtained performance IQ scores within the average range, and case **HW $_L$6** encountered difficulties beyond simple conjunction search, despite an intact right hemisphere and PIQ within the average range. It is also possible that recovery periods may have precluded demonstration of neglect. Recovery periods in patients used in this study were longer than the window of recovery time in which neglect is usually observed (Cassidy 1999, Jehkonen 2000), and Ferro (1990) suggests that recovery from neglect is particularly rapid after injury sustained during childhood. Two other possibilities must be considered regarding the lack of neglect after right hemispherectomy. Previous work suggests that right hemisphere dominance for attentional function develops gradually (Dobler 2001, Corballis 1995) hence it remains possible that visual cognitive functions in the isolated right hemisphere of left hemispherectomy patients may not have achieved sufficient levels of maturity to demonstrate superior performance, perhaps as a result of crowding. It is also possible that removal of the diseased hemisphere enabled expression of compensatory abilities of the intact hemisphere that are usually inhibited by default activation of a particular pathway, even when it is damaged (Plourde and Sperry 1984), an attractive hypothesis that is revisited in later chapters.

4.6.3 One versus two functional hemispheres

Scores were broadly similar between patient and control groups for simple attentional tasks, but differences emerged on search tasks requiring generation of a search strategy within a random A3 array, which suggests that as task demands increase, the gulf widens between individuals completing a task with one versus two hemispheres.

In addition to similar levels of performance in the isolated left and right hemispheres, patients and controls also demonstrated a similar range of line bisection strategies and magnitude of bisection errors. It is acknowledged however, that there was a trend towards more patients obtaining scores below the cut off level for this task, and controls obtaining higher age equivalent scores though results did not reach statistical significance. Visual search performance was also similar in patients and controls when tasks involved simple conjunction search for salient targets as in the star cancellation test and subtest A of the balloons test. This implies that visual search with a lone hemisphere is as timely and efficient as two hemispheres on simple search tasks.

There were also no differences between patients and controls on the sky search task, unlike the other serial search tasks that were based on an A3 array. This did not confirm the prediction in section 4.2, which stated that patients and controls would differ on complex search tasks. Whilst the distractor: target ratio of the Sky Search test is relatively intermediate within the selection of tasks used in this study, the nature of target discrimination is more complex, involving comparison of paired stimuli. The nature of paired target selection appeared to slow the search process relative to other tasks but overall detection rates are similar across groups and all groups varied widely in terms of performance. It is possible that the orderly arrangement of stimuli in the sky search task emphasises the selective attention process as opposed to combined execution of search strategy and selective attention, which accords with Mort and Kennard's (2003) proposal of automated or pre defined search strategies reducing the burden on spatial working memory. Although the columnar arrangement of stimuli may encourage a systematic search, it may still be serial in nature and thus laborious, which may increase time per target scores. It is also possible that more haphazard search patterns are employed, thus bypassing the opportunity to execute a search pattern that places minimal demands on attentional resources via the prespecified columnar arrangement. This would result in a self generated search process that involves complex discrimination between pairs of targets and distractors, that will in turn, burden the executive system and result in an ineffective search. Lack of group differences between patients and controls suggest that both scenarios were prevalent in each group, resulting in a similar spectrum of performance. If the above assumptions were correct, time per target scores would increase due to individuals performing effortful serial search and others engaging in unstructured haphazard search. Indeed, this was illustrated in figure 4.9.

Ineffective search strategies may explain poor performance in subtest B of the balloons task. As the array seems to be random, a self generated search process is executed amongst an array of salient distractors that are nine times as numerous as targets, which are also perceptually less distinct. The resulting search will be slow and serial, and if unsystematic, will result in poor target detection rates. It is possible that both patients and controls adopted these strategies, leading to rapid, efficient detection rates in some individuals and slow, relatively inefficient detection rates in others. This may account for the wide variability in scores observed in all groups. Differences emerged between patients and controls in terms of total score and time per target on subtest B of the balloons test, which suggests that the isolated hemisphere has more difficulties mediating visual search when task demands increase. This is exemplified by the fact that almost all adult hemispherectomy patients were below the cut off level on this subtest compared to only a third of control subjects within this age range. It seems unlikely that hemianopia created a disadvantage, as time per target rates were similar on the A3 array constituting subtest A of the balloons test and all study participants were above the cut off score. It is also of note that the Balloons task has a time limit of 3 minutes for each subtest. All participants completed subtest A within the time limit, but subtest B was often partially completed at the end of the time limit. Slower time per target rates would therefore result in a lower total score within a specified time limit. A similar pattern of differences (total score and time per target) between patients and controls was also evident on the map mission test, which made similar cognitive demands in terms of serial search within a random A3 array, which further substantiates the possibility that inefficient generation of a search strategy to mediate target selection within a large random array resulted in slower detection rates in patients and thus lower total scores due to imposed time constraints. Figure 4.8 showed that controls tended towards detecting similar numbers of targets in the left and right halves of the array within the time limit, whereas the hemispherectomy patients tended towards higher target detection rates in one half of the array within the time limit. This finding is consistent with slow search rates precluding adequate exploration of both halves of the array within the time limit. Further study is required to record scanpaths and cancellation patterns to substantiate these possibilities.

Differences between patients and controls lend support to the notion of interhemispheric interaction being advantageous in attentional processing (Liederman 1986, Belger and Banich 1998) as it enables division of labour between the hemispheres when task demands are high. It is possible that different aspects of computation are allocated to each hemisphere, thus reducing intrahemispheric attentional load by directing input to different hemispheric resource pools that may function in parallel. The isolated hemisphere is not bequeathed with similar advantages. These advantages are not observed on relatively simple tasks, perhaps due to the capacity of unihemispheric processing being sufficient, thus callosal transfer of information is unnecessary. The callosum is believed to act as a gating mechanism that remains closed when task demands are low, but opens when task demands become increasingly complex and require division of labour between the hemispheres (Belger and Banich 1998). The random A3 arrays used in this study may have appealed to such a gating mechanism, with subsequent reduction in attentional load in each hemisphere in control subjects, and an overburdened isolated hemisphere in patients.

4.6.4 Age at seizure onset and task performance

The positive correlations observed between seizure onset and task performance implies that attentional function may become increasingly resistant to the effects of cerebral insult as development proceeds, though it remains speculative in the light of the inconsistent results observed across groups. The relationship between age at seizure onset and task performance is not particularly clear from the results obtained in this study. It seems possible that patients with later onset of seizures obtain better scores in selective attention tasks and so the left and right hemispheres become more flexible in terms of accommodating visuospatial functions later in childhood, perhaps after the establishment of verbal functions. The relative lack of association between these variables in the study groups remains to be confirmed and possibly elucidated with larger sample sizes.

4.6.5 Summary

In summary, it appears that a broad spectrum of attentional capacity may be observed in the hemispherectomised patient population. Whilst some patients remain vulnerable to hemianopia, spatial positioning of stimuli and motor activity, others are able to make accurate spatial judgements regardless of these factors. When considering performance in bisection and visual search tasks, it was of note that none of the right hemispherectomised patients demonstrated neglect, which contrasts with results from studies of patients with focal unilateral lesions. Lack of hemisphere specific differences may result from hemispheric equipotentiality, immaturity of right hemisphere function as a result of global cognitive impairment, or lack of inhibition of the intact left hemisphere. All study participants were able to effectively engage in simple visual search tasks, suggesting that either isolated hemisphere possesses a basic working model of visual attention. Whilst no differences were apparent between left and right hemispherectomised patients, controls outperformed patients on search tasks requiring rapid execution of an efficient search strategy across A3 arrays. These findings imply that absence of division of labour in the isolated hemisphere may hinder performance in tasks requiring complex visual search. Further study is required to investigate these possibilities.

5 Processing facial information

5.1 Introduction

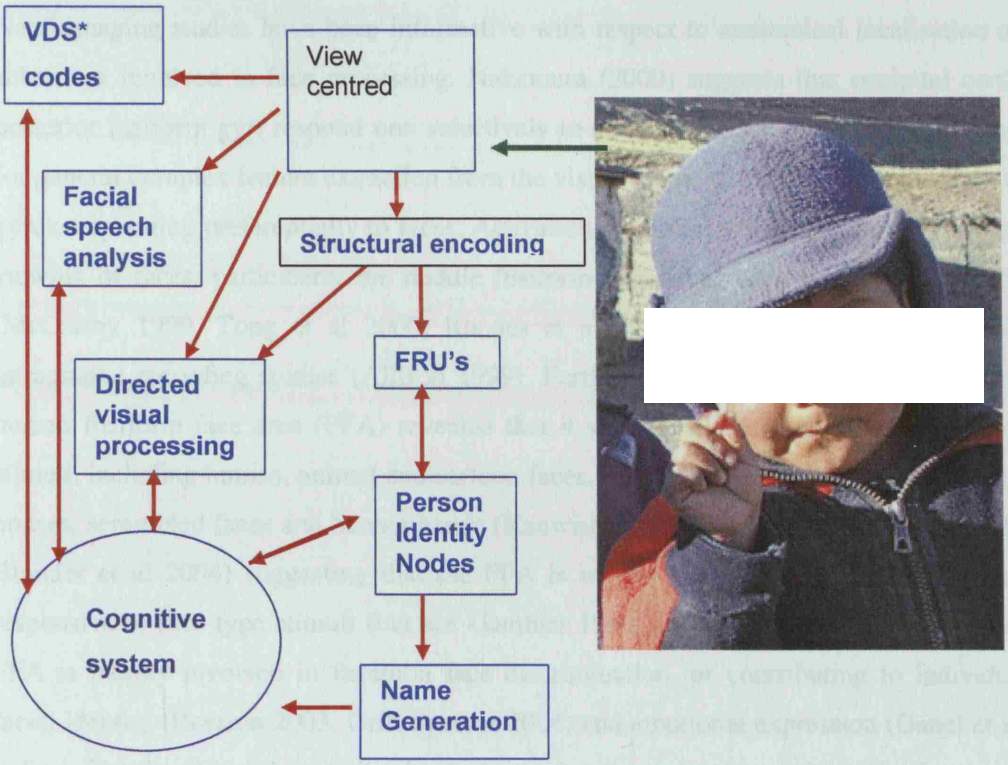
An overview of the literature concerning neuroanatomy, laterality and development of face processing suggests that hemispherectomy for injuries sustained during childhood may provide an interesting model with which to address the inherent capabilities of the left and right hemispheres to subserve this complex and socially vital function. The following chapter is based on experiments that examined the integrity of face processing after hemispherectomy. The Bruce and Young model was used to parse face processing into different elements that were amenable to investigation. The extraction of visually derived semantic information, formation of structural codes and activation of face recognition units were the focus of this study, in addition to examining the strategies that underlie successful individuation of faces.

5.1.1 The Bruce and Young model of face processing

The significance of the face as a biological and social signalling mechanism was remarked upon by Darwin in 1872, who described the ubiquity across species of utilising information conveyed in the face. The process of extracting information from a face was modelled almost two decades ago by Bruce and Young (Bruce and Young 1986). The components of the model are still extremely useful and relevant as a method of conceptualising the hierarchical stages of face processing, from initial registration of input to recall of relevant information.The model is summarised in figure 5.1. The entry level stage of face processing is the pictorial code, which is a view dependent snapshot of the face. Changes in viewing angle, lighting, expression or accompanying attributes such as hairstyle or facial hair render the previous pictorial code useless for making a successful attempt at identification, but successive pictorial codes of a particular face can be summated into a structural code that withstands such changes. It is these codes that mediate everyday recognition of familiar faces, and recognition of recently encountered, relatively unfamiliar faces. The structural code forms a representation that can be compared to stored templates, with activation of face recognition units (FRU's) and subsequent generation of the feeling of familiarity if a match is obtained.

Whilst structural codes enable detection of familiarity, there is a wealth of information that can be extracted from both familiar and unfamiliar faces. Visually derived semantic codes pertain to general information that is not identity specific and may be viewer centred, such as age, gender, emotion, attentiveness and intention.

Figure 5:1. Bruce and Young's face processing model (*VDS = visually derived semantic).



Visually derived semantic codes may be contrasted with identity specific semantic codes that contain information specific to a particular individual such as occupation, social connections, the viewer's relationship to the person and so on. Although these codes are not always regarded as being qualitatively different, instead reflecting the strength of the semantic code along a continuum of meaningfulness (Rhodes 1985), Bruce and Young draw the distinction based on the assertion that each type of code is based on different kinds of information. Visually derived semantic codes are derived from what is physically observed in a facial stimulus at that moment in time, whereas identity specific semantics often have a relatively arbitrary association with the surface form of the face. In addition, identity specific semantic codes are linked to recognition of a particular individual via person identity nodes (PIN's) within the model, whereas visually derived semantic codes are not.

The final step in Bruce and Young's model of face recognition is the retrieval of the appropriate name code for the familiar face. The notion of a separate name code as distinct from the identity specific semantic code is derived from the fact that the experience of recognising a person without being able to remember their name is a frequently observed event (Reason and Mycielska 1982, Young, Hay and Ellis 1985, Abdel-Rahman 2004), and dissociations between recognising and naming have been observed in patients with cerebral injuries (Farah 1990).

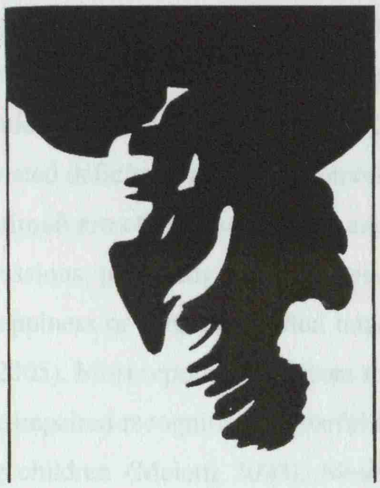
5.1.2 The structural and functional anatomy of face processing

Neuroimaging studies have been informative with respect to anatomical localisation of neural substrates involved in face processing. Nakamura (2000) suggests that occipital cortices and posterior fusiform gyri respond non selectively to complex visual stimuli, and are responsible for general complex feature extraction from the visual scene, with a region in the right fusiform gyrus responding preferentially to faces. Activation of ventral extrastriate cortex during passive viewing of faces, particularly the middle fusiform gyrus, has been consistently demonstrated (McCarthy 1999, Tong et al 2000, Rhodes et al 2004), which accords with results from intracranial recording studies (Allison 1999). Further investigation of this region, termed the human fusiform face area (FFA) revealed that it was equally responsive to a variety of face stimuli, including human, animal and cartoon faces, as opposed to weaker responses for objects, houses, scrambled faces and human hands (Kanwisher 1996, 1997, Puce 1996, McCarthy 1997, Blonder et al 2004) suggesting that the FFA is indeed face selective, or at least maximally responsive to face type stimuli (but see Gauthier 1999, 2000). Debate exists as to whether the FFA is merely involved in face/non face discrimination, or contributing to individuation of facial identity (Rossion 2003, Grill-Spector 2004) and emotional expression (Ganel et al 2005). Indeed, functional imaging studies have shown that the recognition of familiar faces selectively activates the fronto-temporal cortex (Sergent *et al.*, 1992, Gorno Tempini *et al.*, 1998 Leveroni *et al.*, 2000), including inferior temporal regions (Andrews et al 2004). Interpretation of facial expression of emotion is believed to occur in anterior temporal structures, such as the amygdala and anterior temporo-parietal cortex (Adolphs 1994, Whalen 1998, Baas et al 2004). This implies that ventral stream processing of faces bifurcates into 1) processing of semantic and biographical information within postero-inferior temporal cortices, and 2) processing of affective information within a substream located more anteriorly. This accords with separation of these attributes in the Bruce and Young model, and was demonstrated in a recent fMRI study (Winston et al 2004). At present, the neural basis of other types of visually derived semantic processing such as age and gender estimation remains to be elucidated by neuroimaging studies.

In addition to localising the anatomical substrates of face processing, there is also a considerable amount of literature regarding the nature of its functional basis. Diamond and Carey (1986) distinguish between three different kinds of information involved in the face recognition process: (a) isolated features such as nose, mouth etc, (b) first order relational features that specify basic relationships between parts such as the position of the eyes in relation to the mouth, and (c) second order relational features that represent subtle and distinct relationships between elements of the first order configuration. Rhodes (1993) suggests that although a general feature based encoding process is responsible for initial stimulus registration, individual identification of faces is made explicit via coding of second order relations, perhaps as a result of calculating deviations of the stimulus face from the default schema. Rhodes refers to this as norm based coding, which accords with the prototype model proposed by Goldstein and Chance (1980) outlined in section 5.1.3.

Yin's (1969) pioneering account of the face inversion effect provided early support for the assertion that although face recognition may be mediated by featural or configural processing, it is the latter form of processing which predominates. It is now an established finding that neurologically intact individuals are both slower and less accurate when attempting to identify faces that have been turned upside down. Inversion disrupts the spatial configuration among facial features, which is more detrimental to recognition than alterations to featural information (Bartlett and Searcy 1993, Carey 1981, Rhodes 1993, Malcolm et al 2004). When greyscale photographs of faces are inverted, adults have difficulty recognising the identity of the face based on spacing of features, but have no difficulty perceiving the stimulus as a face (Friere 2000). Recognition was considerably easier when inverted faces markedly differed according to morphology of features, suggesting inversion effects are most detrimental to second order relations. Moscovitch (2000) found that the inversion effect could be amplified in neurologically intact controls by fracturing familiar faces, thus causing further disruption to configuration. Identification rates fell from 70 to 20 percent, providing further support for the importance of configural, orientation specific information in face recognition. Inversion may also disrupt perception of first order relations when stimuli are sufficiently degraded. Performance on the Mooney closure of faces task (Mooney and Ferguson 1951) is markedly reduced when faces are inverted (Kanwisher 1998, George 2005), as is face detection in paintings such as Archimboldo's Vegetable Gardener (see Figure 5.2). These findings suggest that face *perception* is also aided by orientation specific cues when viewing conditions are less than optimal.

Figure 5:2. Mooney closure faces test example and Archimboldo's vegetable gardener



Debate exists as to whether the inversion effect is specific to faces. Although the object processing system may also depend configural input to a certain degree, it is believed to be a product of piecemeal integration of information about orientation specific local features and categorical relations between them, as opposed to representations of orientation specific contour configurations (Moscovitch 2000).

Comparison of faces with control stimuli for inversion tasks is considerably difficult, as the ideal control stimulus should be equated to faces in terms of class familiarity, psychosocial importance, conventional orientation and configural complexity. Evidence is mixed for polarised objects, as houses do not seem to be susceptible to inversion effects (Haxby 1999), yet positive results have been found for shoes (de Gelder 1998) and complex figures known as greebles (Gauthier 1997). Studies using animal faces with trained experts (Diamond and Carey 1986) demonstrated that dog experts showed a comparable inversion effect when asked to recognise faces and dogs. This suggests that developing expertise within a particular class of stimuli is related to distinguishing between category members on the basis of subtle differences in configural information. Naïve subjects on the other hand, would use feature based strategies, hence there would be no differences in discriminating upright and inverted stimuli. This accords with Gauthier's studies using "greebles", whereby increasing sensitivity to configuration became apparent when subjects had become familiar with stimuli (1997).

Studies of patients with cerebral insults have also provided valuable insight into the structural and functional basis of face processing. Impaired recognition of familiar faces, or prosopagnosia, is a rare phenomenon that provided early impetus for investigating the possibility of face specific regions in human cerebral cortex. As there are multiple stages at which face recognition may become compromised, the resulting deficits will differ according to the stage of processing at which the system fails. Disruption of initial encoding is characterised by failure to extract visually derived semantic information such as age, gender, and emotional expression, yet familiar face recognition may be intact (de Renzi 1991 case GD) or impaired (Tranel and Damasio 1988, De Renzi 1991 case LA). There is a paucity of literature regarding further fractionation of visually derived semantic codes in patients with cerebral lesions with the exception of isolated deficits in processing emotional expressions (Bowers 1985, Adolphs 1994, 1999). Ekman stimuli are often used (Ekman and Friesen 1976) to enable assessment of 6 basic emotional expressions pertaining to happiness, sadness, anger, fear, surprise and disgust. Judgement of happiness or surprise is often intact relative to negative emotions (Mandal 1991, Adolphs 1996, 2005). Most reports come from studies of patients with damage to the amygdala, and demonstrate impaired recognition of fearful facial expressions (Adolphs 1994, 1999, Calder 1996) including children (Meletti 2003). Similar findings are reported in studies of adults

(Leung 1998) and children (Dimitrovsky 1998, 2000) with learning disability. Evidence is mixed regarding differences in perceiving these emotions in neurologically intact individuals, with some authors reporting no differences in recognition accuracy between emotions (Ekman 1976) whilst others report better recognition accuracy scores for happiness relative to fear (Palermo and Coltheart 2004). Disruption of processing beyond formation of structural encoding preserves the extraction of visually derived semantic information and matching unfamiliar faces across different viewpoints, but recognition of individuals is impaired (Benton 1972, Malone 1982, De Renzi 1991 case VA, Ettlin 1992, Mattson 2000, de Gelder et al 2003). Loss of face selectivity of the N170 event-related potential component has also been observed in prosopagnosic patients (Bentin 1999). Disruption of the later stages of processing, at the level of conscious recognition are manifest as recognition deficits, but evidence of covert processing may be apparent (Bruyer 1991).

Studies of patients with cerebral injury accord with neuroimaging studies of neurologically intact individuals that implicate occipito-temporal cortices for structural encoding of facial configurations (De Renzi 1991, Barton et al 2002, Joubert et al 2003). The parahippocampal gyrus is linked to the matching process between perceptual input and stored representations, and the anterior temporal cortex is believed to be the storehouse of identity specific semantic information (Clarke 1997, Crane and Milner 2002). Specificity of the face perception mechanism is supported by double dissociations between patients with visual agnosia that cannot recognise objects yet face recognition abilities are intact (Rumiati 1994, Feinberg 1994, Moscovitch 1997, Buxbaum 1999), and prosopagnosic patients that demonstrate preserved object recognition (De Renzi 1997). The effects of face inversion have been investigated in prosopagnosic patients, findings from which suggest that prosopagnosic patients perform better with inverted faces (Moscovitch 2000, de Gelder 1998). This effect was interpreted as inversion decoupling the damaged holistic processor from the cognitive systems mediating task performance. Upright faces would automatically engage the damaged but still active holistic processor, thus preventing intact feature based processing systems from mediating task performance, whereas inversion does not engage the holistic processor and recognition may proceed by using a piecemeal featural strategy. Support comes from callosotomy patients as the disconnected left and right hemispheres are both able to process upright faces (Plourde and Sperry 1984), suggesting that piecemeal face processing mechanisms in the left hemisphere may be inhibited in patients with focal right hemisphere lesions unless faces are inverted. A similar rationale was proposed in chapter 4 regarding lack of neglect in these patients. It is of note that inverted animal faces and objects may also be processed more effectively when inverted in patients with object agnosia (Valentine 1988, De Gelder 1998), which suggests that a variety of objects besides faces may engage orientation specific holistic processing.

In summary, it appears that face processing may be subserved by distinct but interconnected neural substrates that enable different properties of facial stimuli to be extracted and utilised to yield information pertaining to the codes specified in the Bruce and Young model. Although faces may be processed using feature based and configuration based mechanisms, it seems that orientation specific configural mechanisms are the dominant mode of processing familiar faces in the neurologically intact individual, as evidenced by susceptibility to the inversion effect.

5.1.3 Is there a laterality gradient in face processing?

Evidence for cerebral laterality of function in the domain of face processing has been one of the most consistent demonstrations of right hemispheric specialisation to date. Evidence for right hemisphere superiority in face processing comes from a variety of sources, including tachistoscopic studies (Rhodes 1985) neuroimaging (Kanwisher 1997, McCarthy 1997, George 1999, Rossion 2000, 2003, Noesselt et al 2005), electrophysiological recordings (Allison 1994), and lesion studies (de Renzi 1994, Mesad et al 2003, Joubert et al 2003, Schiltz et al 2005).

There is considerable evidence from studies based on performance of neurologically intact individuals and clinical populations to suggest that facial information is processed differently by the left and right hemispheres. Right hemisphere superiority for faces is generally observed (Rhodes 1985) and is manifest as a left visual field (LVF) advantage for face processing in neurologically intact individuals. LVF advantages have been found for recognising gender (Luh 1991, Burt and Perrett 1997), judgement of emotional expressions (DeKosky 1980, Christman 1993, Magnussen 1994), matching views of unfamiliar faces (Warrington and James 1967) and familiar face recognition (Rhodes 1985). Evidence from callosotomy patients suggests that although either hemisphere can recognise faces adequately, right hemisphere superiority is evident and different hemispheric strategies are apparent that reinforce the conception of the left hemisphere processing stimuli in a parts based manner, with the right hemisphere utilising a holistic method (Levy 1972, Corballis 1998). Configural processing of face stimuli has indeed been associated with a left visual field advantage, whereas face processing that involves the establishment of individual features appears to demonstrate a right visual field advantage (Parkin and Williamson 1987, Sergent 1982). The computation of metric deviations in configuration from a prototype accords with the proposed role of the right hemisphere in computing metric spatial relations (Kosslyn 1989). Imaging studies of neurologically intact individuals suggests that both hemispheres are recruited during face processing, though levels of right hemisphere activation are consistently greater in tasks measuring face/non face discrimination (Puce et al 1996, Kanwisher 1997, Mc Carthy 1997), emotional processing (Gur 1994) and face recognition (Nakamura 2000). Sergent and Signoret (1992) found more selective left hemisphere activation for objects, and right activation for faces. Object classification demonstrated enhanced activity in the lateral temporo-occipital and middle temporal gyrus of the left hemisphere, whereas face classification led to increased activation of the right fusiform, right hippocampal gyrus and bilateral anterior temporal activation.

The inversion effect also supports the notion of complementary processing strategies of the two hemispheres when encoding facial information. The left visual field advantage observed in face processing experiments is abolished when faces are presented upside down (Leehey 1978, Levine 1988). This is paralleled by changes in the N200 over the right hemisphere, which is smaller and of longer latency (McCarthy et al 1999) and results from fMRI studies that demonstrate decreased right hemisphere activation when faces are inverted (Leube et al 2003). The loss of right hemisphere superiority when processing inverted faces may be related to loss of conventional configuration and subsequent reliance on feature based processing, which is more akin to left hemisphere processing methods. Indeed, Aguirre et al (1999) found that inverting face stimuli led to increased activation in left hemisphere brain regions classically associated with object processing. These observations suggest that parts based and configural strategies may be used to mediate face recognition, with the latter being the dominant mode of processing as evidenced by susceptibility to the inversion effect.

Clinical and experimental studies have demonstrated preferential involvement of the right hemisphere in processing visually derived semantic information and identification of individual faces. Right hemisphere advantages have been observed for identification of emotional expressions (Ley and Bryden 1979, DeKosky 1980, Ross 1985, Bowers 1991, Borod 1993, Darby 1993, Noesselt et al 2005), and damage to the right hemisphere can impair perception of emotions (deKosky 1980, Meletti 2003), and imagery for emotion (Blonder 1991, Bowers 1993), with lesions typically situated in temporal and parietal regions (Heller 1993). Electrical (Fried 1982) or magnetic (Pourtois et al 2004) stimulation of right temporal cortices can also disrupt processing of facial expressions. Not all emotions are affected similarly in the event of cerebral insult. Happiness appears to be particularly resistant to the effects of injury, whereas recognition of fear appears to be most impaired (Meletti 2003), although this finding may be due to the inherent difficulties encountered when attempting to distinguish between fear and surprise (Damasio 1994). Adolphs (1996) found that age and performance IQ were correlated with recognition of fear and sadness, which accords with studies reporting difficulties recognising negative emotions in the context of cognitive impairment (Dimitrovsky 1998, Leung 1998). As there are more negative than positive emotions, it remains possible that it is more difficult to distinguish between them. In fact, it happiness is the only distinct positive emotion of the basic seven categories used in most experiments. Almost all happy faces contain the stereotypical signal of a smile, whereas more negative emotions are interpreted from a range of featural signals that may vary substantially between individuals. It remains to be seen whether intermediate expressions such as surprise and neutral are also more easily identified in the context of cognitive impairment, based on their relative uniqueness in being construed as *either* positive or negative. Confusion between fear and surprise could have reduced detection rates for the latter expression, and results for neutral expressions are not always reported, hence the question still remains as to whether intermediate emotions may be identified more easily than negative emotions. There are no studies to date reporting selective impairment of other types of visually derived semantic information, which accords with lack of precise localisation in neuroimaging studies. Although lesions of the right temporal lobe have been associated with impaired performance on the Closure of faces test (Landsdell 1970, Milner 1980), control tasks were not used to separate the age and gender estimation component from the closure component.

Debate exists as to whether lesions to the right hemisphere are sufficient to cause prosopagnosia. De Renzi suggests that the lesion must be of sufficient size to cause impairment, but not large enough to destroy the specificity of the condition, which may explain why prosopagnosia is a rare condition. Clinical studies almost invariably indicate evidence of right hemisphere disease such as left visual field defects and visuospatial impairments. Damasio argues that bilateral lesions are needed to produce prosopagnosia, as autopsy studies in prosopagnosic patients that showed clinical evidence of right hemisphere damage, in fact had bilateral lesions (Lhermitte 1972, Meadows 1974, Benton 1980, Damasio 1982, Nardelli 1982), though one autopsy study (Landis 1988) revealed only right occipito-temporal damage. Further support for bilateral involvement comes from reports of complete achromatopsia in conjunction with prosopagnosia (Quaglino and Borelli 1867, Damasio 1980, Spillmann 2000). It is possible that right hemisphere lesions disrupt the neural network critically involved in face recognition only in conjunction with an atypical condition in the left hemisphere such as acquired disease or subtle developmental anomalies. It is of note that Compton (2002) found that in addition to LVF advantages observed for face processing, interhemispheric interaction facilitated face matching according to identity or expression when task demands increased in complexity, which suggests that face processing may benefit from bihemispheric input.

Other clinical studies provide evidence for selective involvement of right hemisphere damage in prosopagnosia (De Renzi 1994, Landis 1988), and Sergent and Villemure's (1989) case report of prosopagnosia in a right hemispherectomised patient also sustains the debate as to whether damage to the right hemisphere is indeed sufficient enough to produce the deficit, though it is acknowledged that many more patients with right hemispherectomy do not appear to be prosopagnosic, and callosotomy patients do not demonstrate prosopagnosia when faces are presented to the left hemisphere. Thus, although evidence is mixed, it seems that it is certainly possible that damage to occipito-temporal areas of the right hemisphere may be sufficient to cause prosopagnosia. This does not negate the possibility of face processing being bihemispheric in neurologically intact individuals, but the crucial lesion that produces impairment can be unilateral. Absence of prosopagnosia in callosotomy and hemispherectomised patients may reflect expression of compensatory abilities in the left hemisphere that are normally inhibited when the damaged region of the right hemisphere remains in situ and is able to communicate with the opposite hemisphere. Reports that demonstrate face selective activation in the fusiform gyrus when prosopagnosic patients view faces (Hasson et al 2003, Avidan et al 2005) and face selective N170 responses (Harris et al 2005) may reflect default activation of a face processing stream that cannot support discrimination of familiar faces. In summary, evidence suggests that the right hemisphere is preferentially involved in face processing, as illustrated by LVF advantages in neurologically intact individuals and callosotomy patients, and corresponding deficits in patients with right hemisphere damage. Laterality effects are evident for judgements of emotional expression, recognition of familiar faces and individuating unfamiliar faces based on configural information. Exactly when right hemisphere affinity for facial information becomes apparent is addressed in the next section.

5.1.4 The development of face expertise

Although a preference for face type stimuli is evident at birth, the development of the ability to engage in rapid, parallel extraction of information that can be utilised to distinguish between different familiar individuals has a trajectory that spans approximately 12 years (Chung and Thomson 1995, Aylward et al 2005). It is a well established finding that human newborns preferentially orient their gaze towards face type stimuli (Goren 1975, Maurer and Young 1983, Morton and Johnson 1991, Valenza 1996), and this early attentional bias is believed to facilitate the development of face expertise. Goldstein's schema theory (Goldstein and Chance 1980) suggests that as development proceeds, there is an increase of schematic knowledge about faces as a class, which accords with suggestions of a face prototype becoming progressively specific during the first year of life (Nelson 2001). Goldstein suggests that schema efficiency is achieved at the cost of schema flexibility, leading to loss of ability to make discriminations between faces that are discrepant from those usually encountered. Support for these assertions come from infant perception studies that report development of face discrimination skills that may be flexibly applied to other species, an ability that is lost about 9 months of age (Pascalis et al 2002, 2005). Early construction of an orientation specific face schema is supported by the inversion effect being observed in infants aged 4 months (Fagan 1972), with discriminations between two inverted faces emerging at approximately 5 months. In addition to increasing sensitivity to featural and configural information, extraction of visually derived semantic information such as gender and expression from facial stimuli also becomes apparent between 3-7 months (Cohen and Strauss 1979, Nelson 1985, Ludemann 1988, Kotsoni 2001). Recognition of familiar faces becomes increasingly robust after 2-3 months (Nelson 2001). Thus it seems that some of the essential components of face recognition outlined in the Bruce and Young model are operational in the first year of life. Decoding facial expressions improves up to approximately 10 years of age (Camras 1985, Boyatzis 1993), with the characteristic pattern of happiness being mastered first, followed by sadness, then by other emotions, with lowest detection rates for fear (Izard 1971, Markham 1992, Vicari 2000). Indeed, this pattern of mastery mirrors the profile of relative accuracy of decoding in adults (see section 5.1.2 and 5.1.3). Assignment of verbal labels for facial expressions begin to emerge at 2 years of age (Smiley and Huttenlocher 1989), with accurate labelling of happy and sad emerging relatively early, and disgust emerging latest of all (Vicari 2000).

It is now well established that children's ability to recognize upright faces improves steadily with increasing age (Carey and Diamond 1977, Blaney and Winograd 1978, Ellis and Flinn 1990). There appears to be a plateau and sometimes a decline in performance at 12:0-14:0 before improving to adult levels at approximately 16:0, which is also accompanied by similar effects on recognition of houses and flags (Carey 1980, Flin 1985). This has been attributed to a shift in dominant strategy from feature based to configural processing, but the inversion effect is observed much earlier in development and appears to gradually evolve until reaching adult levels between 10-14 years of age, which is believed to reflect an increasing reliance on configural information, as opposed to an abrupt shift in strategy (Mondloch 2002).

Although children are sensitive to the basic configuration of internal facial features (Mondloch et al 2002), discrimination between unfamiliar faces is thought to occur on the basis of featural rather than configural cues (Freire and Lee 2000). External as opposed to internal features are used (Campbell 1995) as evidenced by the paraphernalia effect whereby face recognition declines when items such as hairstyle, spectacles and facial hair are altered (Flin 1985, Pascalis 1994, Baenninger 1994). These strategies are similar to the discrimination strategies of prosopagnosic patients that are unable to engage in discrimination between second order relational features, which suggests that face expertise develops over time, and is manifest as increasing sensitivity to subtle differences in configural relationships between facial features.

Another possibility for the observed trajectories of developing face expertise is an increasing reliance on right hemisphere mechanisms, though left visual field advantages for face processing tasks have been found during infancy. Monocular testing of infants aged under 24 months enables assessment of hemispheric function, as input to the right hemisphere comes primarily from the left eye, and input to the left hemisphere comes primarily from the right eye, with callosal transfer between the hemispheres emerging after 24 months (Liegeois 2000). Infants aged nine months demonstrate more rapid learning effects for face discriminations when stimuli are presented to the right hemisphere (de Schonen 1990). De Haan and Nelson (1997) noted that ERP activity was greater over the right hemisphere when 6 month old infants participated in a face discrimination task. The left visual field advantage for face processing tasks is also present during childhood as studies have noted such advantages in children aged 5:0 (Young and Ellis 1976), 6:0 (Chiang et al 2000), 7:0 (Broman 1978, Marcel and Rajon 1975,Young and Bion 1980), and 8:0 (Ross-Kossack and Turkewitz 1984). It must be acknowledged however that more recent studies using fMRI have failed to find hemispheric asymmetries (Gathers 2004, Aylward et al 2005), instead reporting bilateral activation of the fusiform gyri from 9 years of age, though visual field advantages were not examined.

An attractive hypothesis is put forward by Chung and Thomson (1995) that young children process faces holistically but in a relatively unsystematic manner, thus extracting overall similarity and differences between faces, but failing to individuate according to second order relational information. Older children process faces more systematically, which enables consideration of subtle and complex ratios and relationships between features that result in construction of structural codes, thus interpreting face stimuli in an advanced integrative as opposed to primitive holistic manner (Ross and Turkewitz 1982). Thus infants and young children encode both featural and configural information when processing faces (Cohen and Cashon 2001), but efficient utilization of such information becomes apparent later in childhood. Thus as development proceeds, access to appropriate experience may afford increasing specialisation of cortical circuitry within the ventral processing stream, with subsequent emergence of face expertise that appears to be resident in specific regions of ventral occipito-temporal cortex, as predicted by theories of interactive specialisation. In an elegant series of experiments, Mondloch et al (2002) were able to demonstrate age related changes in using configural information to discriminate between faces. Pairs of faces were presented that differed *only* according to features, spatial configuration or external contour, allowing direct assessment of each of these factors when individuating faces. Results suggest that configural processing may reach adult like levels after 10 years of age, whereas discriminations based on featural or external contour differences approach adult levels at 6 years of age.

The question remains as to whether a critical period exists for development of face expertise. Plasticity in developing neural systems mediating face recognition has been addressed in studies of developmental prosopagnosia. Farah (2000) reports a single case study of bilateral occipital infarction sustained at one day of age. Testing at 16 years of age demonstrated that face processing was impaired relative to object processing, which led to the conclusion that an innate face specific mechanism exists that cannot be compensated by other structures, despite a lengthy recovery period. No data regarding other types of within class discriminations are reported, so it is difficult to confirm impairment of a face specific mechanism. Nevertheless, Bentin (1999) reports a case of developmental prosopagnosia whose N170 response to faces was severely attenuated, yet within class discriminations of non-face categories was intact. Similar results were reported by Kress and Daum (2003). There are several other studies that also confirm that cerebral damage sustained during infancy can cause face selective deficits (Young and Ellis 1989, Mancini 1994, Jones and Tranel 2001, Nunn 2001, de Schonen 2005), though concurrent object processing impairments are sometimes observed (Ariel and Sadeh 1996, Behrmann et al 2005). The presence of face processing impairments after lengthy recovery periods for cerebral injuries sustained in early childhood implies that neural reorganisation of face processing systems may be limited in scope for some individuals, although the range of critical factors governing such limitations remain to be elucidated. Further support for early specialisation comes from Le Grand's (2003) study. He found that deprivation of input to the right hemisphere due to congenital left eye cataracts led to impaired processing of second order relational information in facial stimuli, as evidenced by failure to discriminate between faces that differed specifically in this factor. Discrimination of faces differing in featural information or external contour was similar to controls. Shape matching and visual attention were also within the average range. These findings suggest that whilst some aspects of face processing are unaffected by early deprivation of input to one or both hemispheres, processing of second order relational information may be unique in its dependence on early visual input to the right hemisphere. Of course there are reports that contradict such assertions. Configural processing for both faces and objects was found to be impaired in a study of 5 congenital prosopagnosics (Avidan et al 2005), yet no evidence of right hemisphere damage was visible on MRI. In addition, perinatal unilateral lesions may produce relatively mild effects on face processing abilities (Ballantyne and Trauner 1999), with no obvious disadvantage to children with right hemisphere damage, though configural processing was not specifically tested in this study. Thus it remains possible that the face processing system in children is either more widely distributed or demonstrates capacity for reorganisation in the event of cerebral injury. This is also supported by the absence of focal cerebral lesions in some cases of face processing deficits (Ariel and Sadeh 1996, Nunn 2001, Laeng and Caviness 2001, Jones and Tranel 2001, Avidan et al 2005), and studies that report similar face processing deficits in children with left or right cerebral lesions (de Schonen et al 2005), which cause problems for theories of early hemispheric specialisation. It must be acknowledged that reports of developmental prosopagnosia are uncommon, and may therefore account for the current lack of consensus between studies as to lesion specificity and long term functional outcome.

5.1.5 Face processing after hemispherectomy

Face processing capacity in the isolated left and right hemispheres cannot be reliably ascertained from studies of patients with focal unilateral lesions for reasons discussed in chapter 1 (see section 1.4), namely the problems resolving the issue of intra versus interhemispheric reorganisation of function. Studies of callosotomy patients suggest that either hemisphere can recognise faces, though right hemisphere superiority exists. Hemispherectomised patients provide an ideal model in which to investigate the integrity of face processing in the isolated left and right hemispheres, yet there is a dearth of studies to date. Evidence for face processing impairments after hemispherectomy is mixed. Left hemispherectomised patient MP was impaired at matching unfamiliar faces, extracting visually derived semantic information such as gender, age and emotion, and recognizing familiar faces as compared to age and IQ matched controls (Marriotti 1998). Vanlancker (2004) reported intact familiar and unfamiliar face recognition, and preserved age and gender discrimination in the Mooney Closure of Faces task (Mooney 1951) in a left hemispherectomised patient with age appropriate IQ scores. Other reports that include face processing measures in left hemispherectomised patients have demonstrated impaired unfamiliar face recognition in some cases (Ogden 1989 case JSY, Strauss and verity 1983) and intact performance in others (Ogden 1989 case KOF). Additionally, Ogden (1989) reports impaired performance on the Mooney Closure of Faces task in left hemispherectomised patients KOF and JSY, but no control task is given that would isolate either the closure element or the extraction of age and gender from undegraded photographs. Ogden also reported impaired identification of emotional expressions in her study, as did Strauss and Verity. Both of these studies used stimuli from the Ekman and Friesen set.

There are 5 studies that report performance on face processing tasks after right hemispherectomy. Whilst Smith (1969), Damasio (1975) and Chiricozzi (2005) report no apparent difficulties with familiar and unfamiliar face recognition in each of their right hemispherectomised cases, Strauss and Verity (1983) report a case that had difficulties matching different views unfamiliar faces and identifying emotional expressions, and Sergent and Villemure (1989) report the only case to date of prosopagnosia in a right hemispherectomised patient. Whilst age and gender discrimination were intact, slight confusion between negative emotions became apparent, a tendency that was also apparent though to a lesser degree in controls. Unfamiliar face matching across different views was slow but accurate, but recognition of familiar faces was severely impaired. It becomes apparent that only 3 studies directly measured the ability to process familiar faces, with intact performance in

Damasio's right hemispherectomised patient (Damasio 1975), and pathological results being obtained in left hemispherectomised patient MP and right hemispherectomised patient BM (Marriotti 1998, Sergent and Villemure 1989). Further research is needed using a larger study sample and a detailed battery of assessments to examine different aspects of face processing in these patients.

5.1.6 Aims and general predictions

The principal aims of this neuropsychological study of face processing were (1) to characterize the nature and extent of any impairment in this domain in patients and controls; (2) to determine the relationship between side of hemispheric injury and task performance; (3) to determine whether face processing is more efficient when mediated by two functional cerebral hemispheres; (4) to determine the relationship between age at onset of seizures and task performance.

Between groups comparisons of neuropsychological data from the patient and control groups were carried out. The predictions were as follows:

- Hemispherectomised patients and controls were expected to have a basic working model of face processing as defined by Bruce and Young, based on the hypothesis that either hemisphere can mediate face processing and the infrequency of developmental prosopagnosia.
- No differences are expected between patients and controls due to lack of evidence supporting interhemispheric co-operation as a necessary prerequisite for face processing.
- The right hemispherectomy group is expected to demonstrate greatest impairments in face processing tasks that benefit from processing of second order relations based on previous work that suggests right hemisphere dominance.
- Inversion effects are most likely to be attenuated in the right hemispherectomy group when faces differ according to configural information.
- Evidence of prosopagnosia will be unlikely, if cases are found they are most likely to be from the right hemispherectomy group.
- A relationship between age at onset of seizures and face processing test scores is expected in left hemispherectomised patients, based on the possibility of early lesions disrupting the development of non-verbal skills.

5.2 Methods and results

5.2.1 Extraction of visually derived semantic information - methods

5.2.1.1 Estimation of age and gender

The Closure Faces Test (Mooney and Ferguson 1951) was administered to provide a measure of the ability to extract age and gender information from incomplete facial configurations. The test consists of 2 sets of pictures of faces and heads that consist only of shadows rendered in black and highlights rendered in white (see figure 5.2). Each picture measured 9.5cm (length) x 8cm (width). Set 1 comprised 21 even numbered items of the original full set of 48 (3 even numbered items were omitted due to perceptual ambiguity as advised by Lansdell 1968), and set 2 comprised the 24 odd numbered items. Subjects were presented with three practice items followed by test cards one at a time and asked to decide whether the face presented on the picture card was a girl, a boy, a grown woman, a grown man, an elderly woman or an elderly man. Each set of cards had 4 examples of each of the six categories. Subjects scored one point for each face correctly identified by age and gender, producing a maximum of 21 points for set 1 and 24 points for set 2. Scores were also calculated for gender (items where either gender alone or age and gender had been correctly identified), and age (items where either age alone or age and gender had been correctly identified). Age and gender scores each had a maximum of 45 possible points. Although the original testing procedure specified by Mooney (1957) and Lansdell (1968) required subject to sort cards into the six response categories by placing them in appropriate labelled boxes, this was not feasible for the current study as most of the patient group experienced reading difficulties. Response choices were thus repeated verbally for each card and the subject responded verbally. Predictions for this task are as follows:

- The right hemispherectomy group may perform more poorly than left hemispherectomised patients and controls, based on previous observations of impairments on this task after right hemisphere lesions (Landsdell 1968, Milner 1980).
- No dissociation between age and gender based errors were expected, based on lack of isolated deficits reported in previous studies, and small focal lesions that may cause dissociation are not present.

The photographic age and gender identification test (PAGIT) was designed to provide a measure of age and gender estimation from intact black and white photographs of faces, thus providing an approximate control task for the Closure of faces test. The structure of the task was designed to resemble the Closure Faces Test as closely as possible, so that the closure factor could be isolated as a source of difficulty. A set of 48 (8 in each category of the Closure Faces Test) black and white photographs each measuring 9.5cm (length) x 8cm (width) were presented sequentially in random order on a 15 inch monitor of a laptop computer using presentation software, at a viewing distance of 40 cm. Each photograph was cropped to obscure the hairline pattern, thus any judgements made could be attributed to the face as opposed to hairline. Viewing time was unlimited, though subjects were prompted to make a response if 30 seconds had elapsed since stimulus onset. As in the Closure Faces Test, subjects were required to decide whether the face presented on the picture card was a girl, a boy, a grown woman, a grown man, an elderly woman or an elderly man. Subjects scored one point for each correct answer, producing a maximum of 48 possible points. Scores were also calculated for gender (items where either gender alone or age and gender had been correctly identified), and age (items where either age alone or age and gender had been correctly identified). Age and gender scores each had a maximum of 48 possible points.

Predictions for this task are as follows:

- Scores will be similar across groups due to the removal of the closure element that may have selectively disadvantaged right hemispherectomised patients.
- No dissociation between age and gender based errors were expected, based on lack of isolated deficits reported in previous studies, and small focal lesions that may cause dissociation are not present.

5.2.1.2 Recognition of emotional expressions

A facial expression identification task was administered to provide a measure of the ability to identify the seven basic facial expressions in the set of faces used by Ekman and Friesen (1976) in their classic cross cultural study. 10 faces of each category (Happy, sad, angry, fear, surprise, disgust, neutral) were selected from the original Ekman and Friesen set that had adult inter-rater reliability ratings of at least 90 percent. 9.8cm (length) x 6.5cm (width) photographs of faces were presented sequentially in random order on a laptop computer, at a viewing distance of 40cm. Subjects were reminded of the seven categories upon presentation of each face and asked to select the most appropriate term to describe the emotional expression conveyed by the face. Subjects scored 1 point for each correct identified emotion, producing a maximum of 70 possible points.

Predictions for this task are as follows:

- Happy faces will be more accurately identified than faces conveying negative emotions in all groups, as based on previous findings that illustrate the uniqueness of this emotional expression.

- Surprised and neutral faces will be more accurately identified than faces conveying negative emotions in all groups, based on their relative uniqueness.
- Right hemispherectomised patients will perform more poorly than left hemispherectomised patients and controls for fearful faces in accordance with previous findings of right hemisphere lesions resulting in impaired perception of fear.

5.2.2 Extraction of visually derived semantic information – results

NB. Covariates in chapter 5 ANCOVA models are age at test and PIQ unless stated otherwise

5.2.2.1 Estimation of age and gender

Table 5.1 and Figure 5.3 show the results obtained for the Closure faces test. Repeated measures ANCOVA was used to compare scores on age and gender components of this test, using *face* (2 levels pertaining to age and gender scores) as a within subjects factor and Hemisphere (Right, Left) by Group (Control, Patient) as between subjects factors. Statistical analysis revealed no significant differences between scores for age and gender for any of the study groups, which confirms the prediction in section 5.2.1.1 for this test. The prediction of lower overall scores in the right hemispherectomy group for this task was not confirmed.

Normative data from the Incisa (1994) and Crane (2002) studies were used to examine scores obtained in patients and controls in relation to neurologically intact populations. 11 hemispherectomised patients (8 left: **KY_L1, RG_L3, EBT_L4, JS_L5, HW_L6, NW_L9, PD_L10, TS_L11**; 3 right: **DN_R2, SN_R5, EBK_R10**) obtained age appropriate scores (score within one standard deviation of the mean for the relevant age group). 11 of the 19 control subjects also obtained age appropriate scores. Fishers exact test revealed no significant differences in the frequency of patients and controls obtaining age appropriate scores.

Table 5.1. Closure of faces test scores (Mean +/- SEM).

	HY_L	CT_L	HY_R	CT_R
Total score*	31.08 (2.04)	31.45 (1.77)	27.5 (2.28)	30.63 (1.85)
Total age	35.33 (1.16)	35.91 (1.18)	34.6 (1.13)	35.88 (1.55)
Total gender	34.17 (1.82)	35.27 (1.29)	32.8 (1.91)	34.5 (1.24)

- Set 1 total = 21, set 2 total = 24, total = 45.

Table 5.2 shows the results obtained for the photographic version of the age and gender identification task (PAGIT). Almost all participants had detection rates between 70-95 percent on this task. Of the three cases (1 patient, 2 controls) obtaining scores below 70 percent, it is of note that the youngest patient (**MM_R3**) and control subject (**$GP_{CR}3$**) were in this group. Table 5.3 shows results for each of the different categories of the PAGIT. Mean scores for all categories were above chance levels.

Table 5.2. PAGIT scores* (mean +/- SEM). *Total = 48

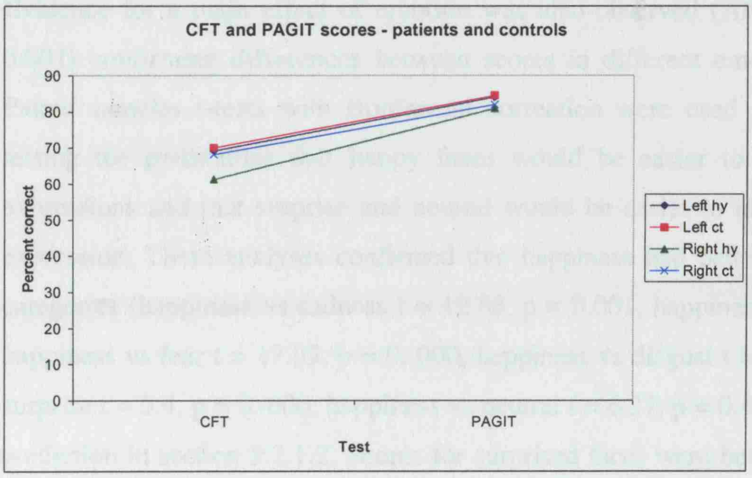
	HY_L	CT_L	HY_R	CT_R
Total	40.27 (0.92)	40.55 (1.11)	38. 8 (1.47)	39.25 (1.83)
Age	43.82 (0.80)	44.18 (0.72)	43.6 (0.88)	43.75 (1.39)
Gender	43.27 (0.69)	43.36 (0.61)	42.5 (1.19)	42.5 (0.98)

Table 5.3. PAGIT scores* by category (mean +/- SEM) *Total for each category = 8

	HY_L	CT_L	HY_R	CT_R
Boy	5.64 (0.47)	6 (0.43)	5.8 (0.47)	6 (0.63)
Girl	5.18 (0.60)	5.72 (0.41)	5.1 (0.31)	5.13 (0.55)
Man	7.64 (0.15)	7.64 (0.20)	7.6 (0.31)	7.63 (0.26)
Woman	6.9 (1.25)	6.09 (0.44)	6 (0.52)	6.5 (0.63)
Old man	7.73 (0.14)	7.55 (0.21)	7.5 (0.31)	7.13 (0.52)
Old woman	7.27 (0.19)	7.45 (0.37)	6.9 (0.67)	6.88 (0.48)

Repeated measures ANCOVA was used to compare scores on age and gender components of this test, using *face* (2 levels pertaining to age and gender scores) as a within subjects factor and Hemisphere (Right, Left) by Group (Control, Patient) as between subjects factors. Statistical analysis revealed no significant differences between scores for age and gender for any of the study groups, which confirms the prediction in section 5.2.1.1 for this test. Repeated measures ANCOVA was also used to compare performance (percent correct) on the Closure faces test and the PAGIT. Within subjects factor of *test* (2 levels pertaining to scores on the Closure faces test and PAGIT) was used. Evidence for a main effect of test was observed (ANCOVA: $F(1, 34) = 14.87$, $p = 0.00$), which suggests scores for the PAGIT were higher than scores on the Closure faces Test.

Figure 5:3. Comparison of performance on the CFT and PAGIT



5.2.2.2 *Identification of emotional expressions*

Table 5.4 and figure 5.4 show the results obtained for the Ekman faces task. Repeated measures ANCOVA was used to examine performance in the seven emotion categories across groups.

Table 5.4. Emotional Expression Identification test scores (mean +/- SEM).

	HY_L	CT_L	HY_R	CT_R
Total /70	44.36 (2.2)	43.54 (3.04)	41.5 (2.38)	40.6 (2.83)
Happy	9.82 (0.22)	10	9.7 (0.15)	10
Sad	4.9 (0.78)	5.82 (0.75)	4.1 (0.59)	5.88 (0.74)
Fear	3.18 (0.69)	6.45 (0.8)	3.6 (0.88)	6.63 (1.02)
Anger	5.54 (0.80)	2.45 (0.84)	7.1 (0.75)	2.38 (0.78)
Disgust	3.63 (1.04)	4.36 (0.88)	2.2 (0.71)	2.88 (1.25)
Surprise	9 (0.49)	7.82 (0.6)	6.9 (0.71)	7.75 (1.21)
Neutral	8.27 (0.70)	6.73 (0.88)	7.9 (0.6)	5.5 (1.02)

Within subjects factor of emotion (7 levels pertaining to scores on each of the emotion categories), and between subjects factors of Hemisphere (Right, Left) and Group (Control, Patient) were included. Evidence for an interaction between emotion and group was observed (ANCOVA: $F(1, 34) = 2.87$, $p = 0.02$), suggesting differences between patients and controls in performance across categories, which is illustrated in figure 5.4. Exploration of this interaction using t tests revealed that patients obtained higher scores than controls for neutral faces ($t = 2.36$, $p = .023$), but this result did not survive Bonferroni correction for multiple comparisons. Evidence of a response bias was evident, as total overall use of the neutral response ($t = 3.2$, $p = .003$) and total incorrect use of the neutral response ($t = 2.9$, $p = .006$) was higher in hemispherectomised patients.

Evidence for a main effect of emotion was also observed (ANCOVA: $F(1, 34) = 6.03$, $p < 0.001$) confirming differences between scores in different emotion categories across groups. Paired samples t-tests with Bonferroni correction were used to explore this main effect by testing the predictions that happy faces would be easier to identify than other emotional expressions and that surprise and neutral would be easier to identify than negative emotional expression. These analyses confirmed that happiness had better detection rates than all other categories (happiness vs sadness $t = 12.88$, $p < 0.001$, happiness vs anger $t = 8.74$, $p < 0.001$, happiness vs fear $t = 17.95$, $p = 0.000$, happiness vs disgust $t = 13.9$, $p = 0.000$, happiness vs surprise $t = 5.4$, $p = 0.000$, happiness vs neutral $t = 6.37$, $p = 0.000$). These results confirm the prediction in section 5.2.1.2. Scores for surprised faces were better than scores for sadness ($t = 6.0$, $p = 0.000$), fear ($t = 9.34$, $p = 0.000$) and disgust ($t = 9.8$, $p = 0.000$). Scores for neutral faces were also better than scores obtained for sadness ($t = 3.18$, $p = 0.000$), fear ($t = 9.2$, $p < 0.001$) and disgust ($t = 7.1$, $p = 0.000$).

Figure 5:4. Ekman faces test category scores.

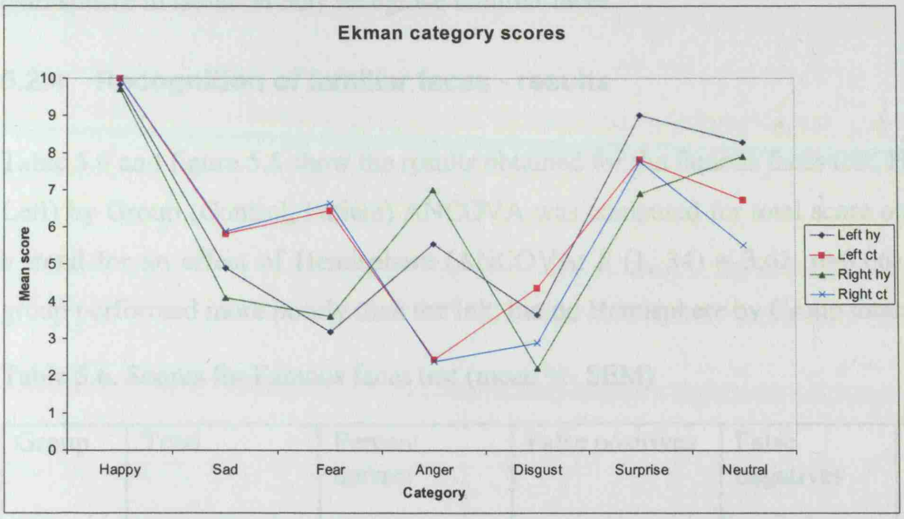


Table 5.5 illustrates differences in detection rates of the different categories of the Ekman and Friesen set used in this study. Confusion between happiness and negative emotions (sadness, fear, anger, disgust) was relatively uncommon, which accords with previous observations.

Table 5.5. Percentage of cases obtaining detection rates of 80 percent or above.

	HY_L (N = 11)	CT_L (N = 11)	HY_R (N= 10)	CT_R (N = 8)
Happy	100	100	100	100
Sad	27	27	0	13
Fear	9	9	0	0
Anger	27	45	50	37
Disgust	18	9	0	13
Surprise	81	72	50	75
Neutral	81	45	60	13

5.2.3 Recognition of familiar faces - methods

A test of familiar face recognition was administered to provide a measure of the ability to correctly identify faces as being familiar or unfamiliar, pertaining to the level of face recognition units in the Bruce and Young model. A set of 30 black and white photographs was sequentially presented on a laptop computer at a viewing distance of 40 cm. All photographs had been cropped to eliminate information other than face and hairstyle. 20 faces were unfamiliar and had been selected from an amateur thespian database. The remaining 10 faces were of famous people (David Beckham, Tony Blair, George Bush, The Queen, Princess Diana, Prince Charles, Daniel Radcliffe/Harry Potter without spectacles, Julia Roberts, Tom Cruise, Jamie Oliver). Subjects were required to state simply whether the face was familiar or unfamiliar to reduce potential disadvantages associated with lesser exposure to media resources. Subjects scored 1 point for each correct answer, producing a maximum score of 30 points.

Scores were expected to be similar across groups based on previous research findings that either hemisphere in isolation may recognise familiar faces.

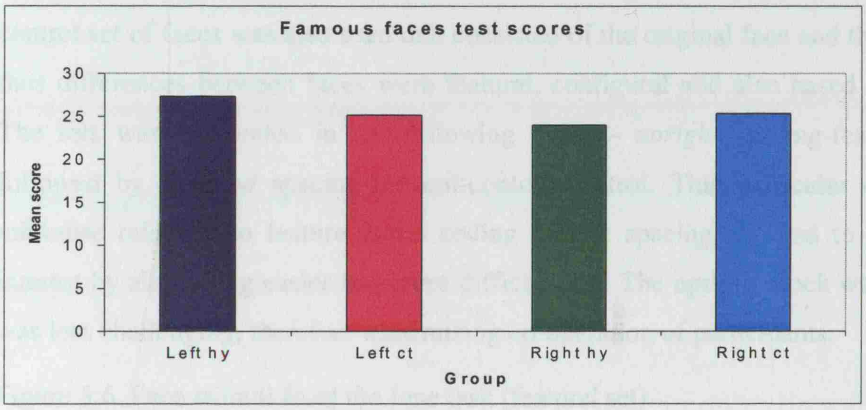
5.2.4 Recognition of familiar faces - results

Table 5.6 and figure 5.5 show the results obtained for the famous faces test. Hemisphere (Right, Left) by Group (Control, Patient) ANCOVA was computed for total score obtained. There was a trend for an effect of Hemisphere (ANCOVA: $F\ (1, 34) = 3.62$, $p=0.06$) because the right group performed more poorly than the left, but no Hemisphere by Group interaction.

Table 5.6. Scores for Famous faces test (mean +/- SEM)

Group	Total	Percent correct	False positives	False negatives	Number of cases < chance (66.7%)
HY_L	27.27 (0.89)	90.91 (2.95)	1.36 (0.53)	1.27 (0.63)	0
CT_L	25.36 (1.03)	84.55 (3. 43)	0.72 (0.27)	3.82 (1.03)	0
HY_R	24 (1.48)	80 (4.92)	2.4 (1.18)	3.5 (0.96)	2
CT_R	24.12 (1.34)	80.42 (4.47)	2.75 (1.05)	3.12 (1.37)	1

Figure 5:5. Famous faces task mean scores



All groups performed well on this task, with only 3 cases (**PP_R1, MM_R3, GB_{CR}1**) obtaining scores at or below chance levels. Chance was set at 66.7% on this task, as it was possible to obtain this score by selecting the "unfamiliar response" on all trials. This was apparent in cases **MM_R3** and **GB_{CR}1**, but case **PP_R1** appeared to respond in a more random manner, obtaining 12 false positives and 4 false negatives. Low false positive rates in the context of false negative rates below 50 percent suggest most patients and controls were able to successfully reject unfamiliar faces whilst identifying faces that appeared familiar. Although not formally required for the purposes of the task, all participants that scored above chance levels volunteered semantic information for faces identified as familiar, thus confirming that selected famous faces were indeed familiar.

5.2.5 Featural, configural and external contour processing of upright and inverted faces - methods

The Jane task (Mondloch, Le Grand and Maurer 2002) was administered to provide a measure of the ability to individuate upright and inverted faces using featural, configural (spacing) or external contour cues. Three sets of test faces were provided by Mondloch and associates, each set containing 30 pairs of faces, with each pair being printed onto a landscape oriented A4 sheet of white paper. Face stimuli for the featural, spacing and contour sets were created by modifying digitised greyscale image of a Caucasian female adult. The models wore surgical caps and did not wear jewellery or glasses, thus encouraging processing of the internal features of the face. Twelve new face stimuli from one face were created: four for each of the three sets. For the spacing set, the position of the eyes was moved up, down, closer together or farther apart, and the mouth was moved up or down relative to the original. The four faces in the featural set were created by replacing the models eyes and mouth with the features of different females. Selected features were of a similar size to the original to minimise resulting changes to the second order spatial relations. The four faces in the contour set were created by pasting the internal portion of the original face within the external contour of four different female faces. A control set of faces was also used that consisted of the original face and three different females, thus differences between faces were featural, configural and also based on external contours. The sets were presented in the following order – *upright* spacing-featural-contour-control, followed by *inverted* spacing-featural-contour-control. This particular order was chosen to minimise reliance on feature based coding for the spacing set, and to maintain participants interest by alternating easier and more difficult sets. The upright block was presented first as it was less challenging, therefore maximizing co-operation of participants.

Figure 5:6. Face stimuli from the Jane task (featural set).

Each picture measured 10.16cm in width and 15.24 cm in length and was presented at a viewing distance of 100 cm. Subjects were required to examine each pair of faces and to state whether the two faces were the same or different. There were 15 "same" pairs and 15 "different" pairs in each test set. (5 test faces per set, thus 10 possible "different" combinations and 5 possible "same" combinations). The control set contained 16 "same" pairs and 16 "different" pairs (4 test faces per set, thus 6 possible "different" combinations and 4 possible "same" combinations). Normative data for children and adults was provided by Mondloch directly. Subjects scored one point for each correct answer, producing a maximum of 30 points for the test sets, and 32 points for the control set. Chance was set at 50 percent for this task.

The predictions for this task are as follows:

- Scores on upright feature and control sets will be higher than upright spacing and contour sets for all groups, in accordance with previous findings. This effect may be amplified due to presence of cognitive impairment and subsequent immaturity in face processing skills.
- The right hemispherectomy group is expected to demonstrate greater impairments than left hemispherectomised patients and controls when discriminating between faces that differ according to configural information only.
- The right hemispherectomy group will demonstrate a smaller inversion effect than left hemispherectomised patients and controls for the configural and control condition, based on previous findings that orientation specific configural processing is mediated by the right hemisphere, and represents the dominant mode of individuating faces.
- Inversion effects will be relatively weak in the featural condition for all groups, based on previous findings of orientation independent processing of features.

5.2.6 Featural, configural and external contour processing of upright and inverted faces – results

Tables 5.7 and 5.8 show the results obtained for the upright and inverted versions of the Jane task, and are summarised in figure 5.7. A hemisphere (Right, Left) by group (Control, Patient) by set (featural, spacing, contour and control) by orientation (upright, inverted) ANCOVA was computed for this task. There were main effects of set (ANCOVA: $F(3, 34) = 5.1$, $p = 0.007$) and orientation (ANCOVA: $F(1,34) = 8.45$, $p = 0.006$) occurring because overall scores on featural and control sets were better than on spacing and contour sets, and overall scores on upright faces were better than for inverted faces. These effects were qualified by a set by orientation interaction (ANCOVA: $F(3,34) = 5.18$, $p = 0.004$). This interaction occurred because there was an effect of set for upright (ANCOVA: $F(3,111) = 12.14$, $p < 0.001$) but not for inverted faces. Follow up tests showed that for the upright set, as predicted, scores for featural sets and for control sets were higher than scores for spacing or contour sets (p's <0.000), while scores for spacing did not differ from scores for contour or scores from featural from scores for control.

Figure 5:7. The Jane task set scores

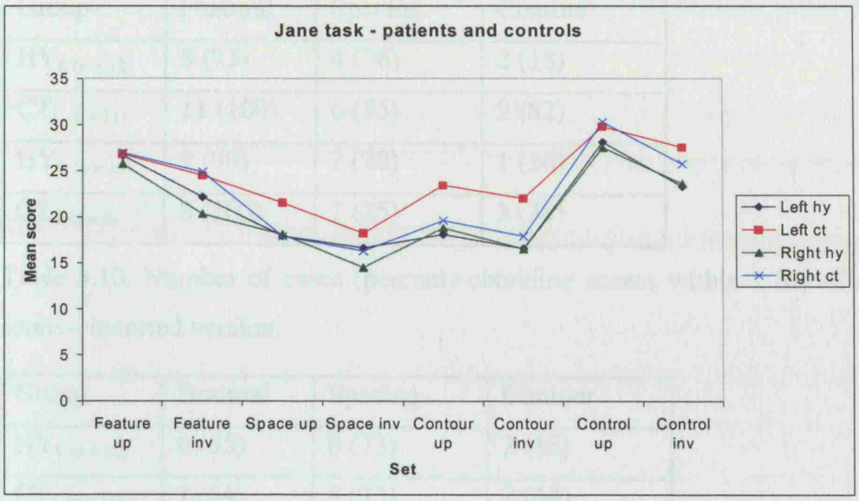


Table 5.7. Scores for the upright version of the Jane task (mean +/- SEM)

Group	Featural	Spacing	Contour	Control	Number of cases < chance (50%)
HY_L	26.63 (0.77)	17.91 (1.22)	18.09 (1.23)	28.09 (1.22)	0F, 3S, 2CT, 0C
CT_L	26.82 (0.93)	21.45 (1.33)	23.36 (1.46)	29.81 (0.74)	0F, 0S, 1CT, 0C
HY_R	25.7 (0.80)	18.1 (0.78)	18.8 (1.39)	27.7 (1.15)	0F, 2S, 3CT, 0C
CT_R	26.88 (0.81)	17.86 (2.02)	19.57 (2.27)	30.29 (0.75)	0F, 3S, 4CT, 0C

F = featural set, S = spacing set, CT = contour set, C = control set

Table 5.8. Scores for the inverted version of the Jane task (mean +/- SEM)

Group	Featural	Spacing	Contour	Control	Number of cases < chance (50%)
HY_L	22.09 (1.56)	16.63 (0.65)	16.54 (1.34)	23.27 (1.54)	1F, 4S, 8CT, 0C
CT_L	24.5 (1.51)	18.18 (1.05)	22.0 (1.61)	27.36 (1.42)	0F, 3S, 1CT, 0C
HY_R	20.3 (1.48)	14.5 (0.60)	16.5 (1.59)	23.8 (1.80)	1F, 7S, 8CT, 1C
CT_R	24.86 (1.14)	16.28 (1.17)	17.86 (1.82)	25.71 (1.78)	0F, 5S, 3CT, 0C

F = featural set, S = spacing set, CT = contour set, C = control set

Tables 5.9 and 5.10 show the number of cases obtaining age appropriate scores on the Jane task (scores within one standard deviation (SD) of mean score for the appropriate age group). It is of note that a proportion of left (**RG $_L$3, JS $_L$5, HW $_L$6, JL $_L$12**) and right (**DN $_R$2, MM $_R$3**) hemispherectomised patients obtained age appropriate scores in both upright feature and spacing sets, which implies that the isolated left or right hemisphere are capable of resolving featural and configural cues in upright faces appropriately.

Table 5.9. Number of cases (percent) obtaining scores within 1 SD of age appropriate mean score – upright version.

Group	Featural	Spacing	Contour
$HY_{L\ (n=12)}$	8 (73)	4 (36)	2 (18)
$CT_{L\ (n=11)}$	11 (100)	6 (55)	9 (82)
$HY_{R\ (n=10)}$	9 (90)	2 (20)	1 (10)
$CT_{R\ (n=8)}$	8 (100)	2 (25)	3 (38)

Table 5.10. Number of cases (percent) obtaining scores within 1 SD of age appropriate mean score – inverted version.

Group	Featural	Spacing	Contour
$HY_{L\ (n=12)}$	6 (55)	8 (73)	2 (18)
$CT_{L\ (n=11)}$	7 (64)	8 (73)	7 (64)
$HY_{R\ (n=10)}$	3 (30)	4 (40)	1 (10)
$CT_{R\ (n=8)}$	8 (100)	4 (50)	1 (13)

Table 5.11. Number of cases (percent) demonstrating an inversion effect*.

Group	Featural	Spacing	Contour	Control
$HY_{L\ (n=12)}$	5 (45)	2 (18)	0	4 (36)
$CT_{L\ (n=11)}$	2 (20)	2 (20)	1 (10)	2 (20)
$HY_{R\ (n=10)}$	4 (40)	3 (30)	1 (10)	4 (40)
$CT_{R\ (n=8)}$	1 (14)	0	2 (29)	2 (29)

* Inversion effect is a difference of 5 points or more between upright and inverted set scores.

Inversion effects for the spacing set were lower than expected in left hemispherectomised patients and controls and right control subjects. The greatest inversion effects were expected for the spacing set, but floor effects appear to have confounded results. As most participants obtained scores approximating chance in the upright version of this set, it is unsurprising that scores on the inverted set were not substantially lower. The contour set was similarly affected by a high proportion of participants obtaining scores close to chance on the upright set. Although higher scores were obtained on featural and control sets, thus allowing for a reduction in score on the inverted set, this was not anticipated due to the nature of the featural individuation cue being relatively impervious to changes in orientation.

5.2.7 Age at seizure onset and task performance

Correlation analyses were run between age at seizure onset and results of each of the assessments reported above. Partial correlations were used to control for age at test where appropriate. For the left hemispherectomy group, positive correlations were found between age at seizure onset and total score obtained on the PAGIT ($R = 0.825$, $p = .002$). Scores on some of the subsets of the Jane task were also positively correlated with seizure onset (Feature set inverted $R = 0.725$ $p = .018$, Global set upright $R = .703$ $p = .023$, global set inverted $R = 0.653$, $p = .041$, Cousin set inverted $R = 0.836$, $p = .003$). There were no other significant correlations for any of the other study groups.

5.3 Discussion

The principal aims of this neuropsychological study of face processing were to characterize the nature and extent of any impairment in this domain in patients and controls whilst considering the relationships between task performance and variables such as side of hemispheric removal, presence of one versus two functional hemispheres, and age at onset of seizures. Overall, results suggest that the basic elements of the face recognition system outlined by Bruce and Young that were investigated in this study appear to be intact. This implies that each cerebral hemisphere is able to maintain and/or develop the necessary circuitry to mediate face perception and recognition as outlined in the model, though development of adult like expertise remains elusive in most cases Both hemispheres were able to extract visually derived semantic information from facial stimuli pertaining to age and gender, appropriately categorise emotional expressions into positive and negative, individuate upright faces based on featural information, and in a small number of cases, also using configural information. Almost all patients were able to distinguish between familiar and unfamiliar faces when task demands on memory and attention were relatively low.

5.3.1 Visually Derived Semantic Information

Results from the Closure of faces test and the PAGIT suggest that the isolated left or right hemisphere is capable of extracting visually derived semantic information from facial stimuli that pertains to age and gender, but extraction rates markedly decrease when stimuli are degraded. Previous studies with hemispherectomised patients or patients with temporal lobe lesions have reported mixed results, some finding impairments with right-sided injury (Lansdell 1968, Milner 1980), some with left-sided injury (Ogden 1989, Marriotti 1998) and some as in the present study, finding no laterality effect (Mendola 1999, Crane 2002). The variability in findings may in part be due to an era effect, whereby the closure task is more difficult when old-fashioned images and hairstyles are used (Crane 2002) an effect that would be particularly salient in children and young adults. The general complexity of the task may also account for why scores were low across all groups. In other words performance seemed related to general level of cognitive ability rather than the presence of one versus two working hemispheres.

Differences between scores on the Closure and PAGIT tasks suggest that closure ability is the key component of impaired performance on the CFT as opposed to difficulties extracting age and gender information from facial stimuli. These results suggest that visually derived semantic information may be extracted from a face in the context of general cognitive impairment. The primacy of these skills is exemplified by their emergence in the first year of life (Kotsoni 2001), and may contribute to their preservation in the context of cerebral injury. It is also of note that that no advantage exists for age based versus gender based discriminations and vice versa, which supports the lack of dissociations reported in previous work. It makes intuitive sense that processing resources for age and gender may be extremely similar, as both involve analysis of morphology of facial features and landmarks such as the thickness of the supraorbital ridge and mandible, the fullness of the lips, and the depth and number of skin creases around regions such as the forehead, eyes and mouth (Bates 2001). The steadfast nature of such discriminations in the face of total unilateral cerebral insult in hemispherectomised patients reflects the fact that visually derived semantic information is extracted in the early stages of visual processing and is thus more likely to be bilaterally represented. Early stages of processing place emphasis on perceptual rather than cognitive resources, which might enable preservation of these skills in the context of generic reduction in cognitive function. These results add to previous hemispherectomy outcome studies (Ogden 1989, Sergent and Villemure 1989, Marriotti 1998, Vanlancker 2004) that collectively include results for just 5 patients on age and gender discrimination tasks.

Results from the Ekman task confirm that basic categorisation of emotional expressions into positive, neutral and negative are possible in cognitively impaired individuals mediating such identifications with an isolated left or right hemisphere, which accords with previous hemispherectomy outcome studies (Strauss and Verity 1983, Sergent and Villemure 1989) and studies of individuals with learning difficulties (Leung 1998, Dimitrovsky 1998, 2000) using the same stimuli. This implies that the expression code postulated in the Bruce and Young model has some degree of integrity in the isolated left or right hemisphere. The results also accord with previous findings in patients with focal unilateral lesions (Strauss and Verity 1983, Adolphs 1996) in terms of happy faces being relatively easy to identify. As happy is the only distinct example of a positive emotion in the set of Ekman faces, it is possible that its relative uniqueness contributed to higher rates of identification. The relative simplicity of positive-negative discrimination is also supported by its pertinence in infancy (Davidson and Fox 1982, Ludemann 1988). The uniqueness principle was used to generate the prediction that intermediate expressions such as surprise and neutral would also be easier to identify than examples of negative expressions, which was confirmed when scores for intermediate expressions were compared to scores for negative emotions. It has been previously suggested that happiness and surprise are easier to identify than other emotions due to the distinct appearance of the mouth in each of these expressions (Vicari 2000). This may also account for lower scores obtained for negative emotions, whereby combinations of upper and lower facial signals must be discriminated to accurately decode the expression.

The lack of discrepancy between scores for left and right hemispherectomised patients for fearful faces is at odds with studies suggesting a right hemisphere specialisation for processing fear (Adolphs 1995), and its basis remains to be elucidated. Although there is no evidence from the Ekman and Friesen study to suggest that fear is especially easy or difficult to identify as compared to other emotional expressions in neurologically intact individuals (Ekman 1976), both earlier (Woodworth 1932) and later (Palermo and Coltheart 2004) reports suggest it is more difficult, and studies with clinical populations suggest perception of fear can be differentially impaired in the context of learning disability or after right hemisphere lesions, suggesting some level of dissociation from other emotions (Adolphs 1995). The most common error type for this category in all groups was selection of "surprise", which is a previously established finding (Damasio 1994, Sergent and Villemure 1989). Confusion between anger and disgust, and sadness and neutrality was also evident across study groups, which attests to difficulties encountered in accurately distinguishing negative emotions from each other in the context of cognitive impairment. Results from hemispherectomised patients with PIQ within the average range demonstrate some dissociation between general level of intellectual function and decoding of emotional expressions. All three patients (**HW$_{L}$6, JL$_{L}$12, EBK$_{R}$10**) scored between 67-75 percent on the Ekman task, even though all stimuli had an inter-rater reliability of at least 90 percent.

Collectively, results from the tasks described above suggest that extraction of visually derived semantic information pertaining to age, gender and basic categorisation of emotional expressions is essentially intact in hemispherectomised patients. Identification of specific negative emotional expressions is hindered by the multiplicity of ways in which such emotion can be conveyed, and limited cognitive resources may operate with coarser default rules that effectively categorise emotional expressions into positive, negative and neutral, which has greater social significance than the ability to make finer grain discriminations within the negative emotion category. Similar results obtained by patients and controls on tests of extracting visually derived semantic information suggest that this is not a product of cognising with a lone hemisphere. Early specialisation of the right hemisphere for processing of negative emotions is not supported, though possible effects could be masked by generic reductions in visual cognitive function resulting in coarse categorisations in all groups. Further experiments that separate perceptual and lexical demands when decoding facial expressions may be illuminating in this respect.

5.3.2 Recognition of Familiar Faces

Results from the famous faces test suggest that the isolated left and right hemispheres are able to recognise familiar faces and successfully reject unfamiliar faces when attention and memory demands are relatively low. Successful rejection of unfamiliar faces is important, as some studies suggest that one manifestation of prosopagnosia in some individuals is the feeling that all faces evoke a sense of familiarity (Farah 1990), due to lack of discriminative ability between faces that are truly familiar and those which are unfamiliar. It therefore seems that the availability of a lone left or right ventral stream after hemispherectomy appears to be sufficient to capitalise on visual experience when building face expertise, even within the context of global cognitive impairment. Results are broadly consistent with callosotomy studies, which report that either hemisphere can recognise faces, and the fact that the majority of hemispherectomy outcome studies do not report prosopagnosia. When considering the Bruce and Young model, it seems the isolated left or right hemisphere is able to formulate structural codes and face recognition units for frequently encountered faces, which are activated appropriately upon subsequent encounters with such faces.

The question remains why there appears to be a dearth of reports documenting prosopagnosia after right hemispherectomy. Although early right hemisphere commitment to face processing is evident (Young and Ellis 1976, Broman 1978, Marcel and Rajan 1975,Young and Bion 1980, Turkewitz and Ross-Kossack 1984, de Schonen 1990, De Haan and Nelson 1997, Le Grand 2003), this does not preclude the possibility of face processing developing in the left hemisphere in the context of large right hemisphere lesions. It must be acknowledged that prosopagnosia is relatively uncommon, and factors such as the size, location and timing of the lesion may be critical. De Renzi (1991) suggests that lesions in pure prosopagnosia are often large enough to produce the deficit, yet small enough not to encroach on other areas that would result in a general reduction of visual cognitive abilities. It may still be possible to detect face recognition impairments in the event of extensive cerebral lesions however, if patients were amenable to assessment, as evidenced by prosopagnosia in right hemispherectomised patient BM (Sergent and Villemure 1989). Another explanation for the apparent rarity of prosopagnosia after hemispherectomy is that bilateral lesions are needed to produce permanent prosopagnosia (Ettlin 1992), whereas unilateral damage may produce a transient deficit. Indeed, recovery from prosopagnosia has indeed been documented. In the 6 cases reported by Landis (1986), 3 demonstrated partial recovery. One of 2 cases reported by Hecaen (1957) also recovered within a few weeks, as did the case reported by Assal (1969). It is thus possible that recovery periods in right hemispherectomised patients have reduced the probability of detecting prosopagnosia. Another point of consideration is that unilateral cerebral injury during childhood may manifest differently to similar injuries sustained in adulthood, with reorganisation of function occurring in the event of available substrates. This may also help to explain why there are a handful of reports documenting permanent face selective deficits after early cerebral lesions, perhaps due to damage to regions critical for development of face expertise. The integrity of familiar face processing in left and right hemispherectomised patients in this study lends weight to the proposition that bilateral lesions are needed to produce prosopagnosia. In turn, the findings accord with the hypothesis that in the face of large unilateral lesions, relevant processing space in the developing brain will be allocated to cognitive functions that are vital for independent survival (Ogden 1989, Marriotti 1998). The ability to recognise familiar faces has obvious social and emotional importance, and face stimuli are encountered constantly. Activity dependent development (Piaget 1969, Johnson 2000) would thus ensure that a cognitive domain of everyday functional significance such as face recognition would attain at least some level of maturity, even when available neural processing resources are scarce and would be normally considered sub optimal for the task at hand.

Only 2 right hemispherectomised cases failed to recognise any of the famous faces in the task. It is acknowledged that case **MM$_R$3** was the youngest participant in the study, and may not have recognised any of the target faces simply due to lack of exposure to relevant media sources. There are inherent problems regarding design of familiar faces tasks for diverse study populations. It is impossible to control for the amount of exposure to media resources in study participants, and this factor will always be a potential confound when celebrities are used as famous faces. This was the principal reason for using the feeling of familiarity as opposed to semantic or name details as a means of assessment, as it is more likely that participants will be more equally balanced in their knowledge of familiar versus unfamiliar faces as opposed to volunteering more precise biographical details. There were no anecdotal reports of difficulty recognising familiar faces for any of the study participants. The response profile of case **PP$_R$1** was seemingly random, indicating some degree of confusion between familiar and unfamiliar faces. Positive responses to familiar faces were not accompanied by semantic details, hence it is difficult to conclude that these faces were successfully recognised, which contrasts with responses from other study participants who spontaneously offered semantic information for familiar faces. Further study with patients obtaining high false negative rates would be informative, using familial and non familial faces that are known to be regularly encountered by each subject.

5.3.3 Individuation strategies

The Jane task was particularly valuable in terms of enabling characterisation of strategies used to individuate faces when visually derived semantic cues were controlled for. One hypothesis was that, though either isolated hemisphere would be able to recognize faces, different information would be utilised by each hemisphere to achieve this objective. In particular, the isolated left hemisphere may process faces primarily based on featural information while the isolated right hemisphere may do so primarily based on configural information. The results, however do not appear to confirm this hypothesis. There were no differences between groups on any of the sets, which did not support the prediction of right hemispherectomised patients obtaining lower scores on the upright spacing set and demonstrating a smaller inversion effect on this set than left hemispherectomised patients or controls. Floor effects must be considered as a possible explanation for this finding, though it is of note that right hemispherectomised case **EBK $_{R}$10** failed to obtain age appropriate scores on the spacing set, despite intact general intellectual function. Previous work suggests that processing of featural cues is less demanding on cognitive resources (Valentine 1991). It could be that configural and contour sets are more challenging for a cognitive system that is relatively immature as a result of extensive cerebral damage due to seizure activity and subsequent surgery. If the face processing system in subjects with severe cognitive impairment did not reach levels of maturity akin to that of children aged 10:0, it is possible that featural processing strategies still dominate the individuation mechanism when processing facial stimuli. Indeed, configural processing appears to emerge relatively late in childhood as the dominant processing strategy, even though its presence can be demonstrated within the first year of life (Cashon and Cohen 2004, Mondloch et al 2002).

The possibility of development of the isolated left hemisphere arresting at this level for visual cognitive functions has been previously suggested (Kohn and Dennis 1984), and results from this study suggest that it may also relate to the isolated right hemisphere in some cases, in addition to control subjects with seizure disorders. These suggestions are borne out by results from repeated measures tests suggesting that sets containing featural cues are completed with high levels of accuracy. The presence of an inversion effect in some cases for featural sets is at odds with general claims that featural information is impervious to the effects of inversion (Leder and Bruce 2000, Collishaw and Hole 2000, Freire 2000, Murray 2000), but accords with previous findings on this particular task, particularly for young children (Mondloch 2002). This observation lends further support to the possibility that face processing in study participants is subserved by cognitive systems that have not reached appropriate levels of maturity.

Scores on the contour sets were particularly poor for all groups, perhaps due to ordering effects, as the featural and spacing sets encourage allocation of attention to internal facial features. There appeared to be an all or none effect regarding performance on this task, as patients that obtained scores close to chance admitted to being unaware of any differences between faces and thus resorting to guesses, whilst in other cases, the difference suddenly became clear after a number of trials had been completed, which elevated scores above chance levels. Cases that detected the difference immediately produced score close to ceiling. Further study using contour cues that are easier to detect may provide more information on detection and utilisation of external contour information to individuate faces in the isolated hemisphere.

It is of note that featural processing was relatively strong in all left hemispherectomised cases, which is at odds with the proposal that the right hemisphere is dominant for configural processing. As mentioned earlier, this could be attributed to a relatively immature face processing system that places less emphasis on mechanisms classically ascribed to the right hemisphere, and thus attenuating lateralised differences. Indeed, 7 left hemispherectomised cases obtained mean scores on the upright spacing set that were greater than 2 standard deviations from the age appropriate mean. This implies that in some cases, the isolated right hemisphere may not develop configural expertise in the presence of a general reduction in cognitive function and coexistent limitations in neural processing space. Results from the right hemispherectomy group contrast with previous findings that suggest an inversion superiority effect emerges after damage to the configural processor in the right hemisphere (Moscovitch 2000, de Gelder 1998). Further conclusions could be drawn using a task that would enable higher detection rates in the spacing set, perhaps by increasing the magnitude of configural differences between faces.

Comparison to control groups produced some interesting observations, which support the proposal that faces are distinguished on the basis of featural information in the event of cognitive impairment. All control subjects performed well on featural and control sets. Performance on spacing and contour sets was relatively poor, which is a similar finding to that observed in the hemispherectomy groups. Of 7 cases obtaining age appropriate scores on the upright version of the spacing set, inversion effects were observed in 2 cases. It is possible that inversion effects in these cases are negated by employment of feature based strategies, as 4 of the 5 cases that were expected to show an inversion effect explicitly stated that the apparent length of the nose was a useful cue in the inverted spacing set, which is a manifestation of the alteration of the distance between the nose and mouth in this set.

Collectively, results from patient and control groups suggest that face processing mechanisms in individuals with cognitive impairment are more akin to those of young children, with greater probability of success on pairs of faces that differ according to featural information (Chung and Thomson 1995), and the suggestion of relative schema rigidity in terms of orientation sensitivity to featural cues (Goldstein and Chance 1980). Exceptions to this general observation lend themselves to the interesting possibility that in the context of childhood cerebral injury, the isolated left or right hemisphere is capable of developing face expertise in the form of sensitivity to both featural and configural information in the presence of more general cognitive impairment, though factors contributing to such developments remain to be elucidated.

5.3.4 Age at seizure onset and task performance

The relationship between age at seizure onset and task performance in the left hemispherectomy group implies that as development proceeds, face processing circuits within the right hemisphere may become increasingly impervious to the effects of functional reorganisation after cerebral injury. This remains speculative in light of inconsistent results across tasks used in this study, but results provide tentative support for the crowding hypothesis, which accords with results in other chapters.

5.3.5 Summary

Collectively the results suggest that the isolated left and right hemispheres are able to extract visually derived semantic information from facial stimuli, individuate upright faces using predominantly feature based strategies, and form structural codes of repeatedly encountered faces that may be matched to stored templates to evoke a sense of familiarity. Findings accord with theories of equipotentiality of the developing brain, and interactive specialisation of this socially important function. Lack of difference between patients and controls suggest that in the context of global cognitive impairment, one hemisphere is just as efficient as two when processing facial information, and thus bihemispheric co-operation is not a vital prerequisite for face processing. Almost all patients were able to distinguish between familiar and unfamiliar faces when task demands on memory and attention were relatively low. Difficulties discriminating between negative emotions, distinguishing faces according to configural and contour cues in the majority of cases and distinguishing between recently encountered and completely unfamiliar faces are most likely a result of generic reduction in cognitive function resulting in a relatively immature face processing system.

6 Spatial processing

The human visual system can represent an object's spatial composition and position via multiple frames of reference. There are two principal co-ordinate frames of reference for processing spatial aspects of the visual scene. Egocentric co-ordinates define spatial parameters centred on the observer's body or between the observer's body and objects in the surrounding environment. Allocentric co-ordinates define spatial relations within and between objects around the observer (Priftis 2003). These objects can also be specified relative to the environment, to their own intrinsic structure, or to other objects in the environment. Moreover, objects can also be mentally transformed within such reference frames. In this chapter a series of tests will be used to assess different aspects of spatial processing: Left-right discrimination (section 6.1), Mental rotation (6.2), and Metric and Categorical Spatial Judgements (6.3).

6.1 Left – right discrimination

6.1.1 Introduction

The ability to discriminate between left and right is a crucial milestone in the development of spatial awareness of self, others, and the environment. It also affords communication of simple categorical spatial relationships to others via a common frame of reference. There are a variety of strategies that may be employed to identify left-right orientation of body parts. Body parts that are oriented in the same position as the observer and thus provide a back view, may be identified as left or right by simple egocentric mapping of one's own body parts to those of the visually presented stimulus. When visually presented body parts are viewed from the front, the left and right side must be identified either by mentally rotating oneself to match the viewpoint of the presented stimulus or vice versa. Aside from rotational strategies for left-right discrimination of body parts, it may also be possible to use symbolic representation or prepositional functions that are based on rules pertaining to translation of frontal views of body parts to match the observer's perspective, e.g. a rule of opposites, such that a hand presented on the left side of a body in frontal view will correspond to the right hand of the observer. This use of tacit knowledge enables a relatively rapid analytical strategy as opposed to the more time consuming strategy of mental rotation.

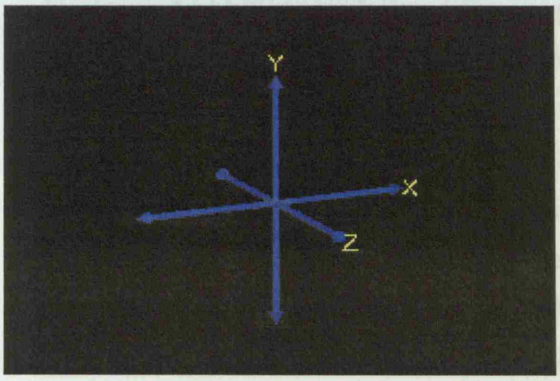
6.1.1.1 The anatomy of left-right discrimination

Data from studies of neurologically intact individuals and patients with cerebral lesions provide converging evidence for parietal lobe involvement in left-right discrimination. Left-right discrimination tasks typically involve identifying left and right body parts on oneself and on a picture of a person facing towards or away from the subject (Semmes 1963, Benton 1994). A small number of functional imaging studies using neurologically intact subjects implicate posterior and inferior parietal lobe activity, particularly the left parieto-temporo-occipital (PTO) region, in mental transformations involving imagined transformations of bodies from an egocentric perspective (Hannay 1983, Parsons 1995, Bonda 1995, Kosslyn 1998; Zacks, 1999). If bodies are inverted, the pattern of lateralisation changes with right hemisphere regions becoming more involved (Zacks, 1999; Ratcliff, 1979), possibly due to mental rotation of the images (Kosslyn, 1998). This suggests there is a system that depends on cortical tissue in the PTO region that mediates transformations necessary to imagine changes in the position and orientation of the body relative to objects around it.

In addition to results from neuroimaging studies, left hemisphere mediation of left-right discrimination using an egocentric frame of reference is generally supported in studies of patients with cerebral injury (Fournier del Castillo et al 2000, Ohtagaki et al 1998, Oki et al 1995, Garty et al 1989). Lesions to areas near the PTO junction can lead to body scheme disturbances and impaired spatial rotation (Hecaen 1956, Salanova 1995). A deficit in egocentric judgements of left and right on ones own body is known as autotopagnosia and is associated with left parietal lesions (Ogden 1985, Semenza 1988). Deficits in left – right discrimination in adults have been associated with Gerstmann syndrome (Gerstmann 1932), which is also related to damage of the left temporo-parieto-occipital junction (Benton 1959, Mayer 1999). Left-right orientation confusion has been demonstrated in aphasic and non aphasic (Sauguet 1971) patients with left hemisphere damage. The latter observation, in conjunction with the fact that other dimensions in space may be distinguished relatively easily, led Critchley (1951) to conclude that right –left confusion is a spatially rather than linguistically based deficit. A similar conclusion had been reached in the 19th century, when Badal (1888) described left-right confusion in patients with cerebral injury, attributing such confusions to a disorder of spatial reasoning.

It seems that spatial processing can fractionate into Cartesian co-ordinates of *x*, *y* and *z* (Figure 6.1), as evidenced by specific difficulties when engaging in left-right discrimination and thus encoding directional changes along the *x* axis. Case GR (Priftis 2003) sustained a right temporo-parietal injury. He demonstrated impaired discrimination of mirror images of objects about the *y* axis and thus directional coding along the *x* axis. Further investigation revealed impaired directional coding along the *x* axis within allocentric space, yet similar discriminations in other axes of reference were intact. Turnbull et al (2004) also report selective impairment of mental rotation about the y axis in a case of traumatic brain injury, though the locus of the cerebral lesion was not specified.

Figure 6:1. The three Cartesian axes



Ratcliff (1979) found that when left-right discriminations must be made for inverted figures, adult patients with right posterior lesions made more errors in the inverted trials than patients with left sided or bilateral lesions. These findings, in conjunction with right hemisphere lateralisation for inverted figures in the fMRI study mentioned previously (Zacks 1999), suggests that right hemisphere injury may play a part in defective left-right judgements when mental rotation is required e.g. when figures are inverted. It is also possible that right hemisphere function is involved when judgements are required using allocentric co-ordinates such as left-right judgements on a confronting person (Priftis 2003) as these require mental rotation about the y axis to reach accurate left-right decisions. Studies using spatial memory tasks have linked the right hemisphere to allocentric spatial processing (Maguire 1998, Abrahams 1997, Galati 2000, Feigenbaum and Morris 2004), though tasks did not specifically focus on left-right discrimination. It must also be acknowledged that several studies demonstrate impaired left-right discrimination using allocentric co-ordinates in patients with left hemisphere injury (Astur et al 2002). Left posterior lesions have been associated with poor performance on left-right discrimination tasks requiring judgements made on a confronting (facing the observer) person in upright orientation (de Renzi 1985, Semmes 1963). Gold (1995) reports a patient with lesions in the region of the left angular gyrus that demonstrated specific difficulties making left right discriminations on a confronting person, which appeared to relate to difficulties translating his egocentric frame of reference onto the confronting person. Whether these impairments relate to impaired mental rotation about the Y axis, or the final step of mapping left and right from ones own perspective after rotating self or stimulus remains to be elucidated.

When considering results from neuroimaging and clinical studies, it therefore seems possible that two spatial processing systems are involved in left-right discrimination, one involved with egocentric perspective transformations and lateralised to the left hemisphere, and the other concerned with mental rotation and allocentric spatial judgements that is lateralised to the right hemisphere. This possibility is supported by reversal of posterior lateralisation when making discriminations on upright and inverted figures as evidenced in neuroimaging studies, and left and right cerebral lesions producing different spatial deficits pertaining to manipulations within egocentric and allocentric spatial reference frames. Further studies are needed to substantiate or indeed refute the possibility of lateralisation of function for different types of spatial processing, as evidence is tenuous at present due to conflicting conclusions from patients with left (Gold 1995) and right (Priftis 2003) hemisphere lesions. Although some of the available evidence from clinical studies suggests that difficulties with left-right discrimination may manifest differently according to the side of the lesion, definitive conclusions cannot be made in patients with focal lesions regarding the capacity of the isolated left and right hemispheres to mediate left-right discrimination. Hemispherectomised patients would provide a valuable model in which to study possible hemispheric differences in left-right discrimination using ego and allocentric spatial reference frames and to investigate the integrity of left-right discrimination in the isolated hemisphere. Difficulties with left-right discriminations may also arise as a result of global reduction in cognitive function (Strichart 1978), hence any conclusions regarding performance in such tasks must take into account general levels of cognitive function.

6.1.1.2 The development of left-right discrimination

Piaget's classic studies of cognitive development are still extremely relevant in terms of conceptualising the development of the awareness of spatial relationships. He proposed that sensorimotor experience contributes to construction of a schema of the external environment as children move under, over and around objects in space. Experience of the relationship between objects and self and objects in relation to each other contribute to increasing awareness of spatial relationships, and subsequent decentration from egocentric frameworks, illustrating a shift from concrete and subjective representation to an abstract and objective framework of visuospatial cognition. Sensorimotor impressions are believed to contribute to conceptual reasoning of spatial relations, which emerge around 7:0, as evidenced by 5-6 year old children consistently utilising their own view in both perception and imagination tasks, even when asked to imagine the view of others from different positions (Piaget and Inhelder 1948). These skills are of crucial importance when learning to make distinctions between left and right.

The first stage of development of the left-right concept is related to increasing awareness of lateral orientation, based on the symmetry of the body as defined in the sagittal plane. Each half receives a name - " left" and "right" (Benton 1968, Corballis and Beale 1976). These labels are reinforced by increasing awareness of asymmetry such as the use of a dominant hand and thus establishment of an internal reference point used for orientation along the horizontal axis (Lacoursiere page 1974, Corballis and Beale 1976). An early egocentric framework is established for left-right discriminations based on the child's viewpoint by approximately 6 years of age, with efficient execution of crossed commands e.g. touch your right ear with your left hand by 8 years of age (Clarke and Clonoff 1990). The proposal of bodily asymmetry providing a foundation for the development of left-right discrimination is supported by studies in hemiplegic patients who demonstrate global cognitive impairment, yet scores on left-right orientation tests may be significantly higher than other neuropsychological assessment measures (Benton 1968). The basis of this performance is thought to be related to the unilateral motor deficit enhancing the awareness of sideness, and thus accelerating the potential to develop awareness of left and right. Several studies (Benton 1959, 1968, Evans 1975) have reported that patients with hemiplegia also demonstrated superior left-right discrimination skills on confronting figures, with higher scores than controls matched for age, gender and IQ.

The idea of asymmetry providing an impetus for development of the left-right concept can be extrapolated to other axes. Up-down and front-back often have considerably less symmetry than left-right and stronger sensory cues, with gravity defining the former and distinct visual cues defining the latter. Indeed, these distinctions are mastered before the left-right concept (Irwin 1977, Benton 1968, Phinney 1979), with front-back and up-down discriminations being evident in children as young as 4 years of age (Rudel and Teuber 1963, Craton 1990). The relative difficulty making left-right discriminations is also evident in adults, with faster reaction times for up-down discriminations than left-right discriminations (Maki 1979). Rigal (1994) noted that left and right are considerably less concrete than other axes, and thus remain a cognitive concept. Children must learn that left and right are not absolute but relative to the orientation of a referent in space that may change at any moment depending on the current trajectory of both self and object. The lack of natural cues pertaining to left and right lead to delayed acquisition of these concepts and appropriate use of verbal labels. Linguistic ability is not the crucial problem, as up/down and front/back are no more difficult as words yet these concepts are mastered earlier.

Once the application of left and right terms to self is accomplished, these terms are transferred to objects and people in the environment, using self as a central reference point and mapping corresponding half spaces onto external objects. Rigal (1994) notes that transposition by translation occurs by 8 years of age, as children are able to map their own left right orientation to persons facing the same way. The next stage of development in left-right discrimination involves mental rotation to accommodate the application of left and right to perspectives other than the child's. Objects can thus be to the left of or to the right of another object, which may be calculated using allocentric co-ordinates. Mental rotation of objects emerges before mental rotation of persons (Inagaki 2002), as evidenced by elementary mental rotation skills applied to external objects such as ice cream cones in children aged 6:0. As rotation skills increase, decentration becomes more apparent, with appreciation of others viewpoints. Mental rotation tends to be utilised when perspective to be taken from another viewer is greater than 90 degrees in rotation to the child, and is evident by 10 years of age, though it does not mature until at least 12 years of age (Swanson and Benton 1955, Rigal 1994). Taking a perspective different from ones own entails internal spatial transformation that involves mentally re-aligning ones egocentric frame of reference with an external perspective, a cognitive task which appears to be more challenging than rotating external objects in space. This may be related to variation in task demands, with most mental rotation tasks requiring rotation of an external object to an upright position along the z axis and then performing an egocentric left-right judgment, whereas tasks requiring left-right discrimination on another person requires rotation of self or other in the y axis before the left-right distinction can be made. It is also possible that graded development of rotational skills in different axes occurs, with mental rotation in the z plane emerging before rotation in the y plane. The separation of Cartesian axes was mentioned in section 6.1.1.1 in terms of the vulnerability of y axis rotations in the event of posterior cerebral lesions. It seems that most studies demonstrate similar developmental trajectories of the left- right concept when using body part stimuli (Boone and Prescott 1968, Whitehouse 1980, Rigal 1994, Ofte 2002). Own body confusions are very rare after age 6, indicating early establishment of an egocentric reference frame for making left-right discriminations. Although many 5 year old and most 6 year old children can identify right and left with respect to their own body parts, errors are still apparent when both sides of the body are involved, or when considering allocentric representations of left and right. Egocentric reference frames and their transposition to others facing the same way are essentially in place at the age of 9:0, and allocentric left-right discriminations reach adult levels of competence in children aged 12:0.

There is a paucity of literature on the neural substrates mediating left-right discrimination in neurologically intact children, but reports of egocentric left-right confusion in the context of developmental Gerstmann syndrome document similar left PTO lesions to those seen in adults (Fournier del Castillo et al 2000, Ohtagaki et al 1998, Oki et al 1995, Garty et al 1989). It remains to be seen whether left-right discrimination when viewing inverted figures or using allocentric co-ordinates may be disrupted after right hemisphere lesions sustained in childhood. Partial support comes from studies of temporal lobectomy patients demonstrating impaired allocentric processing after right temporal seizure activity and lobectomy (Abrahams et al 1997), but patient data are collapsed across childhood and adult onset seizures hence it remains to be seen whether laterality effects would remain robust using only the childhood cerebral injury group.

6.1.1.3 Left-right discrimination after hemispherectomy

There have been very few reports of left-right discrimination in hemispherectomised patients. Fleischhaker (1954) reports mixed results from infantile hemiplegia cases, with intact left-right discrimination in left hemispherectomised case VR and right hemispherectomised case DG, but impaired discrimination in left hemispherectomised case LM and right hemispherectomised case AZ. No details of testing procedures were given. Damasio (1975) reported intact left-right discrimination in a right hemispherectomised patient, but no details were given of tests used. Ogden (1989) found that body part left-right discriminations using transpositions and rotation were intact in two left hemispherectomised cases tested with the Semmes (1963) body orientation test during adulthood. When making left-right judgements regarding turns on a road map (Money 1976), case KOF approached ceiling and case JSY obtained a score equivalent to a child aged 12:0. Using similar tests, Kohn and Dennis (1974) found that left and right hemispherectomised patients were able to make accurate left-right discriminations on body parts, but that right hemispherectomised patients were impaired when making left-right discriminations on a road map. In light of Kohn's proposal that spatial maturity of the left hemisphere may not progress beyond that of a child aged 10:0, it is of interest to determine whether the left-right concept has been fully mastered in right hemispherectomised patients, which would imply that spatial skills had in fact reached a level of maturity more akin to a child aged 12:0. Left hemispherectomised patients are also of immense interest, as the crowding concept may render these skills immature in the lone right hemisphere, and there is a robust association between left hemisphere integrity and making left-right discriminations within egocentric space.

6.1.2 Aims and predictions

The principal aims of this neuropsychological study of left-right discrimination in hemispherectomised patients were (1) to characterize the nature and extent of any impairment in this domain; (2) to determine the relationship between side of hemispheric injury and task performance; (3) to determine whether left-right discrimination is more efficient when mediated by two functional cerebral hemispheres versus presence of hemiplegia (4) to address the issue of age at onset of seizures on task performance.

Between groups comparisons of neuropsychological data from the patient and control groups were carried out. The predictions were as follows:

- Left hemispherectomised patients would be more likely to show egocentrically based errors than right hemispherectomised patients and controls.
- Right hemispherectomised patients would be more likely to show allocentrically based errors and errors on inverted items than left hemispherectomised patients and controls.
- Patients may outperform controls due to advantages conferred by hemiplegia.
- Age at onset of seizures will be positively correlated with performance on tests requiring allocentric spatial processing and mental rotation in left hemispherectomised patients as the right hemisphere becomes increasingly impervious to the effects of crowding.

6.1.3 Methods

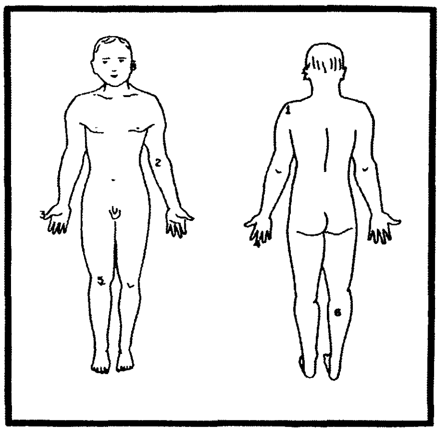
6.1.3.1 Benton left-right orientation test

The Benton Left-right Orientation Test (Benton 1994) was administered to provide a measure of left-right discrimination on ones own body. In addition, the test also measures left-right discrimination on frontal views of a confronting figure. The test consists of 32 items. Items 1-12 require the subject to point to his/her own body parts as a measure of egocentric representation of left and right sides of the body. Items 13-20 require the subject to point to left and right sided body parts on a confronting person, to measure allocentric representation of left and right sides of the body. Items 21-32 require the subject to name body parts on a confronting person that have been selected by the examiner. The demands on motor skill are minimal and hemiparetic patients are able to execute commands with the affected arm. Subjects scored one point per correct answer, producing a maximum of 32 points. The test has a chance level of 50 percent and a cut off score of 27 for children aged 12:0 and above, which also applies to adult scores.

6.1.3.2 Personal orientation test

The Personal Orientation Test (Semmes 1963) was administered to provide a measure of ego and allocentric representations of left-right orientation using front and back views of a confronting person. The test consists of 2 parts, A and B. Each part consists of a series of five diagrams. Each diagram consisted of a front and back view of a man with a series of numbers on various body parts. In version A, subjects are required to touch the parts of their body that correspond with the numbers on the diagram. In this manner, the back view of the figure drawing is identical to the viewer's perspective and thus requires egocentric mapping of numbered parts, whereas the frontal view requires allocentric mapping of the numbered body parts. Version B requires the subject to point to parts of the examiner that correspond to the numbered parts on the figures. In this version, the frontal view is identical in perspective to the view of the examiner and may thus be completed using egocentric co-ordinates, whereas the back view requires allocentric co-ordinates. Each version of the test has 5 pairs of figure drawings, and a total of 35 numbered parts. Scores are computed in terms of total score (1 correct point for each of 35 parts) for version A and B, and the number of errors made in ego and allocentric components of the task. Chance was set at 50 percent for both versions.

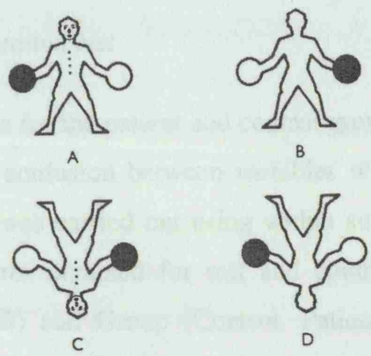
Figure 6:2. Semmes body orientation test (Semmes 1963) – front and back view figures



6.1.3.3 Mental re-orientation test

The Mental Reorientation test (Ratcliff 1979) was administered to provide a measure of left-right discrimination of body parts based on ego and allocentric co-ordinates in conjunction with mental rotation in the Z plane. The test consists of a drawing of a small mannequin that can be shown in one of 4 orientations – upright frontal, upright back view, and inverted frontal, inverted back view. Each of these orientations is repeated 8 times, producing 32 trials. Subjects scored one point per correct answer, producing a maximum of 32 points. The mannequin has a black disc in one hand and a white disc in the other hand. On half the trials the black disc is in the left hand, and on the other half of the trials the black disc is in the right hand. Subjects are required to state whether the black disc is in the left or the right hand. Before the test is administered, subjects are given a simple left-right discrimination test that consists of 12 cards, each with a black circle and a white circle. Subjects are required to state whether the black circle is on the left or the right side of the card. The purpose of this test is to ensure the terms "left" and "right" are used appropriately before administration of the test proper. Chance was set at 50 percent on this task.

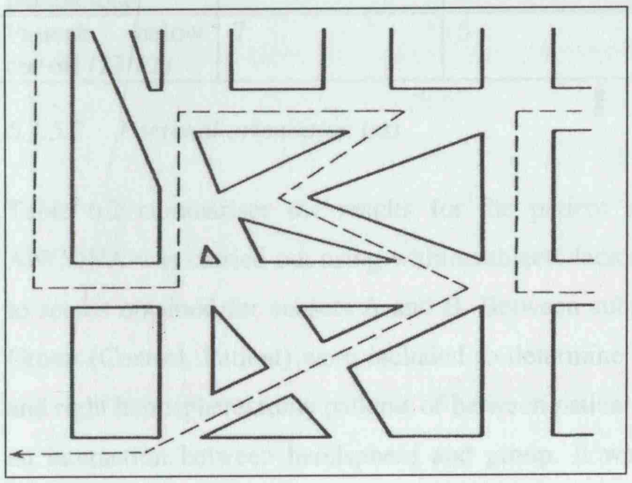
Figure 6:3. Mental reorientation test (Ratcliff 1979) – front and back view figures (upright and inverted)



6.1.3.4 *The Road Map Test of Direction*

The Road Map Test of Direction (Money 1976) was administered to provide a measure of right left orientation in ego and allocentric co-ordinates that is unrelated to body part stimuli. The test consists of a 2 dimensional "road map", upon which a line is traced by a small toy car that encompasses 32 turns. As the line is traced on the map, some turns are made from the subject's perspective; others are made from the examiners perspective, whilst other turns are made laterally. Subjects are required to decide whether each turn is to the left or to the right. Subjects scored one point per correct answer, producing a maximum of 32 points. The cut off score on this task for both children and adults is 22, and chance was set at 50 percent.

Figure 6:4. Road map test of direction (Money 1976)



6.1.4 Analyses

Analyses were carried out as described in chapter 2, section 2.2.4. Age at test and PIQ were used as covariates in ANCOVA models unless otherwise stated.

6.1.5 Results

6.1.5.1 Benton left-right orientation test

Table 6.1 summarises the results for the patient and control groups. Percentage correct for each variable is provided to reduce confusion between variables with different numbers of items. Repeated measures ANCOVA was carried out using within subjects factor orientation, which had 2 levels pertaining to scores obtained for self and confronting items. Between subject factors hemisphere (Right, Left) and Group (Control, Patient) were included to determine whether differences existed between left and right hemispherectomy patients or between patients and controls. There was no evidence for an interaction between hemisphere and group. It was therefore appropriate to look at main effects. Evidence for a main effect of orientation was found (ANCOVA: $F (1, 35) = 18.328$, $p < 0.001$), suggesting lower scores for confronting items across groups. Thus, it seems that the left and right hemispherectomy groups are not selectively disadvantaged in egocentric and allocentric components of this task respectively, and hemiplegia does not appear to confer an advantage on this task.

Table 6.1. Left-right orientation scores - percent correct (mean +/- SEM).

	$HY_{L\ (N=12)}$	$CT_{L\ (N=11)}$	$HY_{R\ (N=10)}$	$CT_{R\ (N=8)}$
Mean	61.5 (8.18)	72.73 (8.85)	65 (9.14)	66.8 (10.79)
Range	34-100	31-100	31-100	25-100
Self orientation	92.36 (3.5)	92.42 (3.45)	90 (5.53)	86.46 (8.62)
Confronting person total	41.7 (13.3)	61.82 (12.47)	50(13.94)	54.38 (14.19)
Patients below cut off (27/32)	7	5	6	4

6.1.5.2 Personal orientation test

Table 6.2 summarises the results for the patient and control groups. Repeated measures ANCOVA was carried out using within subjects factor "subtest", which had 2 levels pertaining to scores obtained for subsets A and B. Between subject factors hemisphere (Right, Left) and Group (Control, Patient) were included to determine whether differences existed between left and right hemispherectomy patients or between patients and controls. There was no evidence for an interaction between hemisphere and group. It was therefore appropriate to look at main effects. Evidence for a main effect of subset was found (ANCOVA: $F (1, 35) = 5.508$, $p = 0.025$), suggesting lower scores for subtest A. Repeated measures ANCOVA was also carried out using within subjects factor orientation, which had 2 levels pertaining to scores obtained for self (Semmes A back view and Semmes B front view) and confronting (Semmes A front view and Semmes B back view) items. Between subject factors hemisphere (Right, Left) and Group (Control, Patient) were included to determine whether differences existed between left and right hemispherectomy patients or between patients and controls. There was no evidence for an interaction between hemisphere and group. It was therefore appropriate to look at main effects. Evidence for a main effect of view was found (ANCOVA: $F (1, 35) = 18.717$, $p < 0.001$), suggesting lower scores for allocentric items across groups. It therefore appears that left and right hemispherectomy groups are not particularly disadvantaged in egocentric and allocentric components of this task respectively, nor are there any advantages conferred by hemiplegia.

Table 6.2. Personal orientation scores - percent correct (mean +/- SEM).

	$HY_{L\ (N=12)}$	$CT_{L\ (N=11)}$	$HY_{R\ (N=10)}$	$CT_{R\ (N=8)}$
Mean A	62.7 (6.75)	65.45 (9.35)	60.57 (7.12)	72.14 (9.75)
Range	37-100	3-100	37-100	37-100
A- frontal view	52.19 (11.2)	52.6 (12.8)	43.16 (10.19)	58.55 (15.58)
A- back view	79.17 (7.71)	85.8 (8.3)	87.5 (5.27)	93.75 (3.34)
Mean B	63.81 (5.22)	75.58 (4.64)	70 (5.67)	78.93 (5.99)
Range	43-100	54-97	45.7 - 100	54-97
B- frontal view	82.5 (5.32)	94.73 (2.56)	84.21 (6.79)	93.42 (3.11)
B- back view	46.9 (8.12)	55.11 (8.21)	57.5 (7.73)	65.63 (8.99)

6.1.5.3 Mental re-orientation test

Table 6.3 summarises the results for the mental reorientation test. Repeated measures ANCOVA was used to examine performance in the upright and inverted items, and the front and back view items. Within subjects factors of rotation (2 levels pertaining to scores on upright and inverted items) and orientation (2 levels pertaining to scores on frontal and back view items), and between subjects factors of Hemisphere (Right, Left) and Group (Control, Patient) were included. There was a main effect of orientation ($F (1, 34) = 6.3$, $p = 0.017$) as overall scores on back view items were better than on front view items. This effect was qualified by an orientation by inversion interaction ($F (3,34) = 22.7$, $p < 0.001$). This interaction occurred because there was an effect of orientation for upright ($F= (1,34) = 34.3$, $p < 0.001$) but not for inverted figures. Follow up tests showed that for the upright set, scores for back view figures were higher than scores for front view figures (p's <0.001), while scores for front and back views of inverted figures did not differ.

Table 6.3. Mental reorientation scores - percent correct (mean +/- SEM).

	$HY_{L\ (N=12)}$	$CT_{L\ (N=11)}$	$HY_{R\ (N=10)}$	$CT_{R\ (N=8)}$
Mean	58.07 (6.10)	72.16 (7.28)	60 (6.63)	64.45 (8.9)
Range	28-94	41-100	28-100	31-100
Upright facing	40.62 (14.03)	55.68 (12.77)	55.56 (14.15)	51.56 (16.27)
Upright back	85.42 (7.02)	93.18 (3.9)	75 (11.41)	79.69 (9.13)
Inverted facing	50 (9.61)	68.18 (10.34)	66.67 (8.07)	60.94 (11.91)
Inverted back	63.54 (9.67)	72.72 (10.09)	47.22 (11.18)	67.19 (12.03)

6.1.5.4 The Road Map Test of Direction

Table 6.4 summarises the results obtained for the road map test. Repeated measures ANCOVA was used to test the prediction regarding scores on items requiring ego and allocentric frames of reference. Within subjects factor rotation (3 levels pertaining to upright, inverted and lateral views) was used, in addition to between subject factors of hemisphere and group. There were no significant differences between scores on upright, inverted and lateral trials across groups.

Table 6.4. Road map scores - percent correct (mean +/- SEM).

	$HY_{L\ (N=12)}$	$CT_{L\ (N=11)}$	$HY_{R\ (N=10)}$	$CT_{R\ (N=8)}$
Mean	63.54 (5.17)	69.60 (5.53)	62.81 (6.93)	73.05 (8.05)
Range	44-97	47-100	41-94	38-100
Inverted trials	57.57 (10.99)	69.70 (6.72)	56.67 (11.17)	61.11 (13.77)
Upright trials	61.82 (9.52)	71.8 (9.23)	66 (10.77)	75 (8.45)
Lateral trials	73.42 (5.81)	68.53 (7.29)	60.77 (6.63)	76.92 (8.72)
Patients below cut off (22/32)	8/12	6/11	7/10	4/8

6.1.5.5 Age at seizure onset and task performance.

Correlation analyses were run between age at seizure onset and results of each of the assessments reported above. Partial correlations were used to control for age at test where appropriate. For the left hemispherectomy group, age at seizure onset was positively correlated with scores on subset A of the body orientation task ($R = 0.65$, $p = 0.043$) and total score obtained on the mental reorientation test ($R = 0.739$, $p = 0.009$). There were no other significant correlations for this group. For the left control group, age at seizure onset was positively correlated with scores on money road map test ($R = 0.847$, $p = 0.03$). There were no other significant correlations for this group. For the right hemispherectomy group, age at seizure onset was positively correlated with scores on subset A of the body orientation task, though results were just outside statistical significance ($R = 0.66$, $p = 0.054$). There were no other significant correlations for this group, and there were no significant correlations for the right control group.

6.1.6 Discussion

The purpose of this section was to assess left-right discrimination abilities in hemispherectomised patients. The principal aims were to characterize the nature and extent of any impairment in this domain, to determine the relationship between side of hemispheric injury and task performance, and to determine whether left-right discrimination was more efficient when mediated by two functional cerebral hemispheres versus any potential advantages conferred by the presence of hemiplegia. It was also important to determine if there was a relationship between age at seizure onset and integrity of left-right discrimination.

6.1.6.1 *The integrity of left-right discrimination within ego and allocentric space*

The results of the various assessments reported in this chapter provided convergent evidence that almost all left and right hemispherectomised patients were able to make left-right discriminations with regard to their own body, and map this perspective onto another person facing the same direction. Left right orientation appears to be challenged however, when mental rotation is required to transpose such perspectives onto a confronting person or map route. Scores on the confronting person items of the Left-right orientation test were lower than self orientation scores for all groups. The same pattern of results was noted for both subtests of the body orientation test and the upright figures of the mental reorientation test. It was of note that scores on inverted frontal items of the mental re-orientation test were not lower than upright frontal items, suggesting that rotation in either z or y axes can pose a challenge for left-right discriminations. Lack of normative data for tasks used precludes detailed discussion on developmental levels achieved by each sub-group, hence scores in relation to chance levels are used as a reference point to discuss whether certain milestones have been achieved by study participants. Consideration of the pattern of performance in individual cases provides general support for the conclusions drawn above and also raises further interesting hints as to how these skills develop at the level of the individual child. The four tests used provide various measures of left-right discrimination in ego and allocentric space that can be fractionated according to processing demands.

Left-right discrimination on oneself was measured by Benton's left-right orientation test, and mapping left and right onto another figure using egocentric co-ordinates was measured by back view figures in Semmes subtest A, back view figures in the mental reorientation test and turns made on the Money road map test. Two patients (**TS**$_{\mathbf{L}}$**11** and **PP**$_{\mathbf{R}}$**1**) had difficulty assigning left-right terms to their own body, but could make discriminations well above chance on a figure facing the same way. This suggests that left-right confusion on ones own body does not preclude accurate mapping of left-right onto external figures. Case **MM** $_{\mathbf{R}}$**3** had the opposite problem of accurate self left-right discrimination but an inability to transpose this perspective onto an external figure. All other hemispherectomised cases were able to perform both functions successfully, suggesting a developmental level of at least 8 years of age with respect to left-right discrimination (Rigal 1994).

Mapping left and right between two external figures using egocentric co-ordinates was measured by front view figures of Semmes subtest B. Case **TS** $_{\mathbf{L}}$**11** was successful despite difficulties in self left-right discrimination. Case **MM** $_{\mathbf{R}}$**3** was also successful despite having difficulty mapping left and right between himself and an external figure. Cases **KY**$_{\mathbf{L}}$**1**, **PO** $_{\mathbf{L}}$**2**, **PD**$_{\mathbf{L}}$**10** and **JL** $_{\mathbf{L}}$**12** had difficulty with this task, despite success on tasks requiring self left-right discrimination and mapping of such perspectives from self to an external figure. Cases **MS**$_R$**7** and **PP**$_R$**1** had difficulty with this task and all subsequent measures, suggesting limits had been reached. It therefore seems that left-right discrimination using egocentric co-ordinates can fractionate into mapping onto self, self to other and mapping between two external figures. All of these functions can develop in the isolated hemisphere, as evidenced by 11 patients (**EBT**$_L$**4**, **JS**$_L$**5**, **LO**$_L$**8**, **HW**$_L$**6**, **NW**$_L$**9**, **DN**$_R$**2**, **GB**$_R$**4**, **SN**$_R$**5**, **TB**$_R$**6**, **KD**$_R$**8**, **BC**$_R$**9**) performing well above chance in all three domains. Collectively, the results suggest that the basic algorithm that computes left-right orientation within egocentric spatial co-ordinates is intact in the majority of study participants, and may be applied to oneself or transposed onto an external figure or map in a similar orientation. This implies a developmental level of approximately 9 years of age with respect to left-right discrimination (Rigal 1994, Ofte 2002). It is also apparent that each component of the concept of left-right discrimination may follow a developmental trajectory that overlaps with other components. Although left-right discrimination on one's own body appears first and foremost, complete mastery of this concept in some cases may take time, thus discriminations involving identification of two body parts such as the command " touch your left ear with your right hand" may emerge later than transposition mechanisms that afford mapping of one's own perspective onto a similar facing external figure, or indeed a map type stimulus. Other cases may demonstrate a protracted course of development for transposition mechanisms, with complete mastery of left-right concept as applied to self before the emergence of transposition of this reference frame from self to other, or between two external figures

Rotating in the z plane then mapping left and right using ego centric co-ordinates was measured using the back view inverted figures of the mental reorientation test. Only 7 patients performed well above chance on this task, and each of them had obtained good scores on at least three of the five measures described above. Thus even when egocentric mapping of left and right is well established, additional demands on spatial processing can obstruct accurate assignment of left and right within egocentric co-ordinates. Of the 7 patients that were successful on this task, cases **EBT** $_L$**4**, **NW** $_L$**9**, and **GB** $_R$**4** scored well above chance on all of the tasks measuring egocentric processing of left and right, suggesting the isolated left or right hemisphere can develop mastery of left-right discrimination within egocentric space, whether such judgements are to be made on oneself, between self and other, between two external figures or when additional demands on spatial processing are apparent.

Mapping of left and right using allocentric co-ordinates on a confronting figure was measured using the Benton left right orientation test, front view figures in Semmes subtest A, front view figures in the mental reorientation test and turns made on the Money road map test. Four left

(**KY$_{L}$1**, **JS$_{L}$5**, **CB$_{L}$7**, **LO$_{L}$8**) and four right (**PP$_{R}$1**, **DN$_{R}$2**, **TB$_{R}$6**, **MS$_{R}$7**) hemispherectomised patients had difficulty on all of these tasks. Whilst it remains possible that **KY$_{L}$1**, **JS$_{L}$5**, **PP$_{R}$1**, **DN$_{R}$2** (aged 11 years 1 month - 12 years 4 months) may go on to develop an allocentric frame of reference for left-right discrimination, the remaining cases are several years beyond the age at which allocentric mapping of left and right is thought to reach maturity, and thus it seems that utilising an allocentric frame of reference for left and right can sometimes remain elusive in the isolated hemisphere. The remaining 13 cases however, were successful on at least one of these four measures (Benton, Body orientation, mental reorientation, road map) of allocentric left-right discrimination, with four cases scoring well on all four measures. These results illustrate that the isolated left or right hemisphere may develop the ability to map left and right using allocentric co-ordinates, albeit to varying degrees of efficacy. It is acknowledged that variation in task demands may have affected success, hence some patients scored well above chance on some measures of allocentric processing and not others. The Benton, mental reorientation and Road map tasks require verbal responses, whereas the body orientation task requires the subject to point to a spatial location on either their own body or the examiners. It is also possible that tacit knowledge was used to complete tasks, thus bypassing rotation and applying prepositions such as a rule of opposites for confronting figures. Due to time constraints, detailed examination of strategies used to complete these tasks was beyond the scope of this study, thus one cannot conclude that good performance on confronting figures tasks is solely due to efficient rotations in the y plane. Further study is needed to address this issue, in addition to collection of normative data to enable more detailed assessment of integrity of function.

Mapping left and right between two external figures using allocentric co-ordinates was measured by back view figures of Semmes subtest B. Five patients (**EBT$_{L}$4**, **HW$_{L}$6**, **JL$_{L}$12**, **GB$_{R}$4** and **KD$_{R}$8**) were successful on this task, all of whom obtained good scores on at least one other measure of allocentric mapping of left and right. These results imply that in a limited number of cases the isolated left or right hemisphere can develop left-right discrimination using allocentric co-ordinates whether the mapping process involves self and external figure, or two external figures. This in turn suggests that the isolated hemisphere can develop or sustain a developmental level of 12 years and above with respect to left-right discrimination (Rigal 1994, Ofte 2002), which is at odds with previous suggestions (Kohn and Dennis 1974) imposing lower limits on left hemisphere maturity for visuospatial skills. This highlights the advantage of using larger study samples to gain a better impression of the spectrum of ability after hemispherectomy.

Rotating in the z plane in addition to using allocentric co-ordinates to map left and right was measured using the front view inverted figures of the mental reorientation test. It is of note that it is possible to obtain full marks on these trials simply by egocentric mapping of self left and right onto the figure without rotating in either z or y axes. This may explain why cases **JS**$_{L}$**5**, and **DN**$_{R}$**2** scored well above chance on this task despite failure to map left and right using allocentric co-ordinates on any other measure. The remaining six cases (**NW**$_{L}$**9**, **PD**$_{L}$**10**, **TS**$_{L}$**11**, **JL**$_{L}$**12**, **MM**$_{R}$**3** and **GB**$_{R}$**4**) had all scored well above chance on at least one measure of allocentric left-right processing, leaving open the possibility of successful rotation in z and y axes, though it is noted that only **NW**$_{L}$**9**, **JL**$_{L}$**12** and **GB**$_{R}$**4** performed well above chance on the back view inverted figures subset. Cases **RG**$_{L}$**3**, **EBT**$_{L}$**4**, **HW**$_{L}$**6** and **BC**$_{R}$**9** performed well above chance on most measures of allocentric mapping but failed this task, suggesting that the demands of mental rotation in both z and y axes may have obstructed their left-right discrimination capacity.

Collectively these results suggest that the isolated left and right hemisphere develops or sustains an egocentric frame of reference for left-right discrimination that may be applied to self, self to other or two external figures. An allocentric frame may fail to develop, but in some cases this spatial reference frame may reach maturity. Three cases (**EBT**$_{L}$**4**, **HW**$_{L}$**6**, **GB**$_{R}$**4**) demonstrated mastery of egocentric and allocentric mapping of left and right on upright figures thus it seems that in a limited number of cases the isolated hemisphere may effectively utilise both types of spatial reference frame. It is acknowledged that sample sizes are small and therefore results are interpreted cautiously.

6.1.6.2 Comparison of left and right hemispherectomised patients

There did not appear to be a relationship between side of hemispheric injury and task performance, thus providing no evidence to support the prediction in section 6.2 that errors in egocentric processing would be more common in left than right hemispherectomised patients or the prediction that allocentric errors would be more common in right than left hemispherectomised patients. These results suggest the isolated left or right hemisphere may develop an egocentric frame of reference that may be applied to different spatial situations via transposition or rotation. There were also no apparent cases of autotopagnosia after left hemispherectomy. These results are at odds with studies claiming that damage to left parietal regions results in impaired left-right orientation from an egocentric perspective (Fournier del Castillo et al 2000, Ohtagaki et al 1998, Oki et al 1995, Garty et al 1989), although data on patients with lesions sustained during childhood is scarce, and individual case data described above provides tentative support for the possibility of left or right hemisphere damage during childhood resulting in impairments in this domain. Right hemispherectomised patients were also no more likely to obtain lower scores than other groups on measures of allocentric processing, which contradicts previous literature that suggest this may be the case. Again it must be acknowledged that right hemisphere affinity for allocentric processing is based on studies of adults, and tests that do not specifically test for left-right discrimination on figures with the exception of the case report by Priftis (2003). Results obtained in this study do not accord with the idea of early hemispheric specialisation for these functions, indeed it seems either hemisphere is capable of developing ego and allocentric mapping of left and right. These findings accord with previous studies of left-right discrimination in hemispherectomised patients (Fleischhaker 1954, Kohn and Dennis 1974, Damasio 1975, Ogden 1989) and support the hypotheses that in the face of large unilateral lesions, available processing space in the developing brain will be allocated to cognitive functions that are vital for independent survival (Ogden 1989, Marriotti 1998). The ability to discriminate between left and right has obvious advantages for building a framework for ones own spatial world and interpreting that of others, and navigating both familiar and unfamiliar environments. Activity dependent development (Piaget 1969, Johnson 2000) would thus ensure that a cognitive domain of everyday functional significance such as left-right discrimination would attain at least some level of maturity, even when available neural processing resources are scarce and may be considered sub optimal for mediating the task at hand.

6.1.6.3 One versus two functional hemispheres

Scores were also broadly similar between patient and control groups for each task. The egocentric items of each of the three "body part" tests were efficiently completed by almost all participants, implying that left-right discrimination on one's own body and translation of this perspective onto an external person facing the same way was essentially intact, with mean scores in each group between 75-95 percent. This confirms that left-right discrimination is impaired on a relative rather than absolute scale in the study sample, and levels of maturity akin to that of a child aged 8:0 have been attained by the vast majority of participants. There did not appear to be any advantage conferred by the presence of hemiplegia which did not confirm the prediction in section 6.2, as scores of the patient groups were similar to controls in each of the assessments carried out.

6.1.6.4 Age at seizure onset and task performance

The positive correlations observed between age at seizure onset and task performance in the hemispherectomised patients did not reveal a strong relationship between these variables, but a small number of positive results implies that patients with later onset of seizures, particularly in the left hemisphere, obtain better scores in left-right discrimination tests. As some tasks did not correlate with this variable, it seems that there is no clear relationship between age at seizure onset and the development of left-right discrimination. These results are interpreted with caution due to small sample sizes, but it remains possible that as development proceeds, the left and right hemispheres acquire left-right orientation concepts that become increasingly resistant to the effects of cerebral insult. These possibilities remain to be elucidated with larger sample sizes.

Overall, the results suggest that the isolated left or right hemisphere can develop an egocentric frame of reference that may be applied to different spatial situations via transposition or rotation. This frame of reference will develop despite global cognitive impairment. A subset of cases may also develop an allocentric frame of reference, which suggests that in the context of childhood cerebral injury, ego and allocentric processing can develop and function efficiently within the same hemisphere. Lack of differences between left and right hemispherectomy groups suggest that either hemisphere may be capable of these developments, which contradicts theories of early specialisation. Comparison with controls suggest that left-right discriminations are not particularly disadvantaged when being computed in the isolated hemisphere, and there does not appear to be any advantages conferred by bodily asymmetries caused by hemiplegia.

6.2 Mental rotation

6.2.1 Introduction

There are three principal axes along which spatial characteristics of an object may be defined, namely top-bottom, front-back and left-right. As objects differ in their respective orientations, same-different judgements become more difficult, and can overburden spatial working memory (Parsons 1987). One way of reducing the burden is to mentally rotate one object to an orientation like that of the other object (Cohen 1996, Shepard and Metzler 1971), as compared to rotating oneself to match the orientation of the stimuli as seen in experiments using body parts as stimuli (see section 6.1).

Most studies of the process of mental rotation involve the discrimination between enantiomorphs (two stimuli that are mirror images). Perception of the precise relationship between two objects usually requires some degree of alignment so that the reflection may be perceived along the axis of greatest symmetry. When enantiomorphs are not systematically aligned, or when only one of them is visible, then some form of mental or physical rotation usually occurs before the enantiomorphic relationship can be perceived. Top-bottom and back – front axes are believed to be resolved first due to their functional priority in establishing canonical orientation, leaving the left-right axis to establish the degree of similarity between the two objects (Corballis 2000). This tendency to regard the left-right axis as relatively arbitrary, in conjunction with the degree of symmetry along this axis, may explain why it is more difficult to make discriminations in this axis, especially for young children. There have been many studies of mental rotation since Shephard and Metzler's (1971) pioneering quantification of the positive correlation between reaction time and the angular rotation of a target from its canonical orientation, a phenomenon that had been noted by Dearborn in 1899. These results have been replicated with a variety of stimuli including alphanumeric characters (Koriat and Norman 1985, Fischer and Pellegrino 1988), amoeba type stimuli (Edelman and Bulthoff 1992), and natural objects (Jolicoeur 1988, 1990). Several authors have also found a relationship between accuracy and angular rotation, with lower scores for larger angular rotations (Smith and Dror 2001, Gauthier 2002, Cohen 1996).

It seems likely that rotations around different axes also place different demands on transformation mechanisms, as rotation in the *z* plane often preserves visibility of features, whilst rotation in the y plane may alter the visibility of features, with some parts coming into view whilst others become occluded. The top-bottom relationship is not violated however, unlike objects rotated in the *z* plane, which may attenuate possible differences in rotation accuracy and speed. Indeed, axis-accuracy relationships have been found for rotated objects (Gauthier 2002). An object may be rotated in one or more axes simultaneously and thus rotations may be successive or performed in parallel (Parsons 1987), depending on the number of axes in which the object deviates from normal. If front-back can be immediately ascertained, then up/down and left/right may be performed simultaneously. Corballis and McMaster (1996) claim that objects must first be rotated to upright before left-right judgements can be made, supporting a stepwise process. Reorientation to a position with a dominant vertical axis is thought to be a necessary pre requisite to the match-mismatch process (Kosslyn 1987, Corballis and Blackman 1990), which contradicts Parsons assertion that rotation may proceed in parallel in all 3 axes.

It is also evident that mental rotation only appears within a certain angular range for some individuals, with a switch in strategy at 180 degrees that attracts a path of minimum cognitive resources to transform the image. Indeed, Jolicoeur (1990) found that RT for stimuli inverted 180 were faster than rotations of 120 degrees, and other studies noted that 2 distinct strategies could be employed to rotate objects, flipping (depth rotation around the x axis) and spinning (plane rotation around the z axis). Flipping was thought to come into play for objects rotated 180 degrees (Murray 1997, Kanamori 2002). The flipping strategy was found to be quicker (Kanamori 2002) and attributed to lack of formation of intermediate representations. Application of tacit knowledge may also come into play at 180 degrees, thus bypassing mental rotation as in left-right orientation tasks discussed in section 6.1.

6.2.1.1 *The anatomy of Mental Rotation*

The most consistent finding in neuroimaging studies of mental rotation to date is bilateral activation of the posterior parietal lobe, particularly Brodmann area 7 and the intraparietal lobule (Alivisatos 1997, Carpenter 1999, Tagaris 1997, Richter 1997, Kosslyn 1998, Zacks 1999, 2003, Jordan 2001, Vanrie 2002, Podzebenko 2005). Area 7 activation is attributed to encoding of spatial relations, allocation of attentional resources, and spatial transformations (Goebel 1998) with SMA activation becoming evident when substantial demands on attention occur (Richter 2000). Relative lateralisation of activity to right parietal areas has been noted in several neuroimaging studies (Deutsch 1988, Inoue 1997, Courtney 1998, Thomsen 2000, Podzebenko 2002, Zacks et al 2003). Alivisatos and Petrides (1997) argue that right parietal activation is related to general visuospatial processing necessary for discrimination of transformed views of stimuli, with activation in left parietal cortex activation linked to active mental rotation of stimuli, an assertion that has been proposed previously (Cook 1994). Their study has been criticised both directly (Harris 2000) and indirectly (Gauthier and Tarr 1997) by studies that favour right parietal lobe involvement. The Alivisatos study used a very limited number of orientations and extensive pre trial practice, facilitating both left hemisphere recruitment in rotation and also stored representations of rotations which substantially increases the risk of bypassing the rotation process in test trials. Several studies (Wendt 1994, Gauthier 2002) found no asymmetry between PTO regions during mental rotation, which implies that mental rotation may depend on co-operation of both cerebral hemispheres. Activation in V5 has also been observed in several studies (Cohen 1996, Barnes 2000, Podzebenko 2002, 2005, Vanrie 2002), and is linked to observations that this region is activated during perception of motion and illusory motion, with regions inferior and posterior to V5 being involved in orientation discrimination, a process that may be indirectly recruited during the performance of mental rotation.

Bilateral frontal activation in premotor cortex has been reported in mental rotation studies (Cohen 1996, Tagaris 1997, Zacks 1999), and is thought to reflect activation of areas involved in motor planning and imagined motor transformations. Activation of area 46 has also been reported, which has been identified as playing a role in spatial working memory (Jonides 1993, Thomsen 2000, Podzebenko 2002, Vanrie 2002), thus activity in this region may occur as a result of holding the rotated stimulus in memory through its various transitions as it approaches an upright orientation. Primate studies demonstrate rich interconnectivity between frontal and parietal areas (Andersen 1990, Chavis 1976, Petrides 1984), which provides a structural basis for fronto-parietal activation observed in mental rotation, in addition to the functional properties of activated regions.

Collectively, results from neurologically intact subjects favour parietal lobe involvement in mental rotation, though it is unclear whether functional laterality exists. Some of the studies mentioned above and the majority of clinical observations argue in favour of a right hemisphere involvement, with comparatively fewer studies supporting preferential involvement of the left hemisphere (Mehta 1991, Vingerhoets 2001). Differences between tasks may be involved, though left hemisphere advantages have been found for alphanumeric and geometric stimuli (Fischer and Pellegrino 1988), and similar advantages have been found for the right hemisphere (McGuinness and Bartell 1982, Ditunno and Mann 1990). Kosslyn (1994) and Corballis (1997) suggest that left hemisphere contribution to mental rotation depends on task complexity. Comparing complex stimuli may occur in a piecemeal fashion by focusing on salient features rather than the overall gestalt, a strategy that is likely to involve the left hemisphere (Corballis 1997). The left hemisphere is also thought to become more adept at mental rotation with practice (Corballis and Sergent 1988, Fisher and Pellegrino 1988). Harris (2000) agrees that overall, the majority of published evidence favours a preferential role for the right hemisphere in mental rotation, with increasing contributions from the left hemisphere according to task complexity and practice. This implies that bihemispheric co-operation may be advantageous for complex mental rotations (three dimensional objects with large angular displacements from upright in multiple axes).

Studies of patients with parietal lobe damage complement findings from neuroimaging studies of neurologically intact subjects by showing that such damage results in severe impairments in tasks that require spatial processing (de Renzi 1982, Ratcliff 1979). Large posterior lesions in patients have been shown to compromise mental rotation (Dee 1970, Ditunno and Mann 1990, Mehta 1987) but the precise areas of parietal cortex involved can not always be ascertained from such studies, hence the value of neuroimaging studies. Patients with right posterior lesions have difficulties identifying objects from unusual views (Warrington and Taylor 1973) and right anterior cerebral artery infarcts that involve the superior frontal gyrus and dorsomedial parietal areas may result in slower mental rotation and impaired visual working memory (Carlesimo 2001). Several studies document impaired mental rotation after right parietal lesions, particularly for large rotations of 120 degrees (Ditunno and Mann 1990, Farah and Hammond 1988, Ratcliff 1979), including patients with intact left-right discrimination in egocentric space (Harris 2000). Kosslyn (1985) and Mehta and Newcombe (1987) report that damage to posterior regions of the left hemisphere may result in impaired mental rotation, though it is of note that no differences were apparent between left and right hemisphere patients when 3D stimuli were used, as both patient groups were impaired relative to controls. Kosslyn (1991) suggests that mental rotation may occur in either hemisphere, with novel stimulus transformations occurring within the metric spatial framework of the right hemisphere, and shifting to the categorical spatial framework of the left hemisphere with practice. The shift from topography to topology enables more rapid processing of image transformations that become increasingly automated and thus further from conscious reflection. It is of note that Zacks et al (2004) report a patient with adult onset right parietal lobe injury who demonstrated adequate mental rotation performance that was associated with increased levels of left parietal lobe activation compared to neurologically intact controls (Zacks et al 2004), which is consistent with the notion that either hemisphere can mediate mental rotation.

Studies with split-brain patients have also contributed to the debate surrounding mental rotation and laterality of function (Corballis and Sergent 1988, 1989, Le Doux 1977). A left field advantage was observed for patients in these studies, and although the left hemisphere improved with practice, it never attained the level of proficiency of the right hemisphere. There are only three studies that have included tests of mental rotation in hemispherectomised patients. Left hemispherectomised patient MP was severely impaired on a task requiring mental rotation of 2D stimuli (Mariotti 1998). Right hemispherectomised patient BM scored above chance levels on a mental rotation task involving rotated 2D alphanumeric characters (Sergent and Villemure 1989). Right hemispherectomised patient GT demonstrated impaired performance on a task requiring mental rotation of 2D shapes to identify assembled 3D objects (Chiricozzi 2005). Single case study designs and disparate tasks across studies prevent detailed statements being made about the ability of the isolated hemisphere to engage in mental rotation, hence it remains to be seen whether the isolated left and right hemispheres are able to engage in rotation of 2D or 3D stimuli in Cartesian x, y and z axes.

6.2.1.2 The development of Mental Rotation

Studies investigating the development of mental rotation in children provide a valuable opportunity to address the concept of metacognition and factors that may contribute to its emergence. Children as young as 3:0 understand that mental images exist and cannot be seen by others, in addition to being different from the physical objects they represent (Estes 1998). Karmiloff-Smith (1992) suggests that metacognition may develop in tandem with conceptual understanding associated with different cognitive functions. Estes (1998) results from a mental rotation task support Karmiloff-Smith's contention, as introspective descriptions of the phenomenon of mental rotation appeared to coincide with the emergence of competence in this particular domain. Non mental explanations were the dominant response type from children aged 4:0, most of who were unable to rotate the figures, obtaining scores of 60 percent. When demands are sufficient, young children simply engage in perceptual matching, as they are unable to anticipate the outcome of the rotation. Six year olds were 83 percent correct, and the majority of children in this age group gave descriptions of the mental rotation process. Most of the adult participants also gave descriptions of the mental rotation process. In contrast to young children, non mental explanations from adults tended to reflect to use of tacit knowledge that enabled the rotation process to be bypassed.

Children and adults do appear to differ in terms of their speed and accuracy of mental rotation. Marmor (1977) found that children aged 5:0 were able to rotate imagined objects when instructed to do so (ice cream cones), albeit more slowly than adults, which was also found by Kosslyn (1990). Five year olds and 8 year olds appeared to be similar in performance though other authors argue that subjects aged 8 years and older behave like adults (Kail 1980, 1985), with the emergence of the rotation-latency relationship emerging at this age (Childs and Polich 1979, Dean 1979, Kail 1980). Childs and Polich (1979) found that reaction time decreases with age from 9:0 – 11:0 – 20:0. This is attributed to general output processing deficiencies as opposed to sluggish rotation, which is supported by the absence of disproportionate increases in reaction times as stimuli depart from 0 degrees. Interestingly, when advance knowledge of the stimulus was given, the adults resorted to a comparative process that bypassed rotation, whereas 9-11 year olds engaged in rotation. This implies application of tacit knowledge occurs beyond the age of 11 years. Waber (1982) agrees that an adult like pattern of function develops between 10-12 years in terms of capitalising on primes and using prepositional information. Increases in speed are attributed to improvement in simple reaction time that is known to occur with age (Span et al 2004). Children aged 13 treat inverted stimuli differently, as indicated by sharp decreases in RT for stimuli oriented 180 degrees. This is due to comparison to a stored image as opposed to engaging in mental rotation. Thus it seems that around the time of puberty, children's skill at manipulating visual images becomes considerably more efficient, leading to simultaneous improvement in both the ability to transform visual images and the ability to utilise imagery in short term memory. There is a paucity of data regarding laterality of mental rotation in both neurologically intact and brain injured children, thus it remains to be seen whether unilateral cerebral injury sustained in childhood produces side specific deficits in mental rotation. Corballis, Macadie and Beale (1985) found a left visual field advantage of rotation of alphanumeric characters in children aged 11-13 years of age, in contrast to a right visual field advantage using the same task in adults (Corballis and McLaren 1984). Booth et al (2000) found that neurologically intact children aged 9-12 years and adults showed bilateral parietal activation when rotating alphanumeric characters, whereas children of the same age with left hemisphere lesions tended towards right hemisphere activation. Further study is needed to determine the impact of unilateral lesions sustained in childhood on the efficacy of mental rotation.

6.2.2 Aims and predictions

The principal aims of this neuropsychological study of mental rotation in hemispherectomised patients were (1) to characterize the nature and extent of any impairment in this domain; (2) to determine the relationship between side of hemispheric injury and task performance; (3) to determine whether mental rotation is more efficient when mediated by two functional cerebral hemispheres, and (4) to determine if there is a relationship between age at onset of seizures and integrity of mental rotation.

Between groups comparisons of neuropsychological data from the patient and control groups were carried out. The predictions were as follows:

- All groups would obtain higher scores on smaller angular displacements as a function of task complexity and generic reduction in cognitive function.
- Performance of patients and controls will be similar on simple trials (2 dimensional rotation, small angular displacement) as callosotomy studies suggest that mental rotation may be mediated by an isolated left or right hemisphere, albeit with different levels of efficacy.
- Right hemispherectomised patients will obtain lower scores than left hemispherectomised patients and controls on harder trials (3 dimensional rotation, larger angular displacement).
- Relevant metacognition will be evident in individuals who have mastered mental rotation.
- Age at onset of seizures will be positively correlated with task performance in the left hemispherectomy group as the right hemisphere becomes increasingly resistant to the effects of crowding.

6.2.3 Methods

The following tasks were designed to build on the results from the mental reorientation test in section 6.1 by encouraging object as opposed to subject rotation, spinning strategies in addition to flipping strategies, application of tacit knowledge, and gradations of rotation as opposed to 0 degrees versus 180 degree inversions. Error rates were used rather than reaction time as previous research has shown that error rates reflect rotation ability in a comparable way to response time (Dror 1997) and speed-accuracy trade off is also less likely (Hertzog et al 1993). Error rates can also provide additional insight into the visual mental rotation process that response times cannot. Chance level was set at 50 percent for all tasks.

6.2.3.1 The Flags test

The Flags test was administered to provide a measure of mental rotation accuracy using 2 dimensional stimuli rotated in the z plane. Three stimulus sets were constructed, each consisting of 5 test cards. Each test card had a picture of the flag of Aruba placed centrally on the bottom of the card, with 4 sample flags placed along the top of the card. The sample flags were rotated in 30 degree increments from the orientation of the target flag, and were either identical to or y axis enantiomers of the target. Subjects were required to state whether the sample flags were the same or mirror images of the target flag. Set 1 contained a total of 20 samples that were displaced by 0-60 degrees from the target. Set 2 contained 20 samples that were displaced by 60-120 degrees. Set 3 contained 20 samples that were displaced by 120-180 degrees. Subjects scored 1 point per correct answer, producing a total of 20 points per set, with a maximum of 60 points for the test. It was predicted that scores on set 1 would be higher than scores on sets 2 and 3 due to increasing task complexity. It was also predicted that right hemispherectomised patients would be more likely to obtain poor scores in sets 2 and 3 as a function of right hemispheric superiority in mental rotation.

Figure 6:5. Flags test (samples rotated 30-150 clockwise from upright)

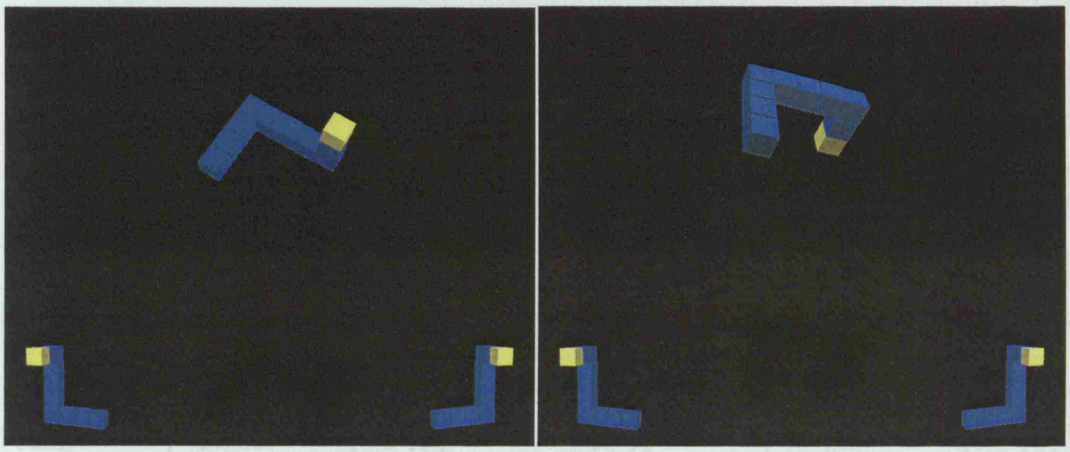
6.2.3.2 Axis one test

The Axis one task was administered to provide a measure of mental rotation accuracy using 3 dimensional Shepard and Metzler type figures that were rotated in 30 degree increments around the z plane. The basic figure was designed to be relatively simple and meaningless in overall three dimensional shapes. The figure consisted of 10 solid cubes attached face to face to form a rigid arm like structure with three right angled elbows, each elbow projecting into a different Cartesian co-ordinate. 11 different perspective projections were created in each axis by rotating the object from 30 - 360 degrees in 30 degree increments. The same set of projections was also created for the enantiomer. There were 66 trials in total (each of the 3 axis sets contained 11 original and 11 mirror image examples). Subjects scored 1 point per correct trial producing a maximum of 66 points. Stimuli were presented in a randomised sequence on a laptop computer. Subjects were required to state whether the centrally placed target figure was the same as the reference figure on the bottom left or its enantiomer at the bottom right of the screen.

6.2.3.3 Axis three test

The Axis three task was designed using the same basic stimulus as the Axis one task, but each target was rotated in a combination of x, y and z axes (for example, 60 degrees in the x plane, 120 degrees in the y plane and 30 degrees in the z plane). 8 blocks of 3 rotation combinations were constructed and mirror imaged to produce the enantiomeric set, producing a total of 48 trials. 2 targets were eliminated due to obscured visibility of the basic structure of the stimulus, leaving a total of 46 trials. Subjects scored 1 point per correct trial producing a maximum of 46 points. Stimuli were presented in a randomised sequence on a laptop computer. It was predicted that right hemispherectomised patients would be more likely to obtain poor scores in the Axis tasks as a function of right hemispheric superiority in mental rotation.

Figure 6:6. Examples from axis one (120^{0z} axis) and axis three (120^{0x} 30^{0y} 60^{0z} axes).



6.2.3.4 Metacognitive awareness of rotation

After the test had been completed, subjects were presented with a test card from set 2 of the flags test and asked to elaborate on the strategy they used to determine the enantiomeric relationship between the target and the samples. A trial from the axis 1 test was also presented and subjects were asked the same question. Comments were collected as an informal record of evidence of metacognition with respect to mental rotation.

6.2.4 Analyses

Analyses were carried out as described in chapter 2, section 2.2.4. Age at test and PIQ were used as covariates in ANCOVA models unless otherwise stated.

6.2.5 Results

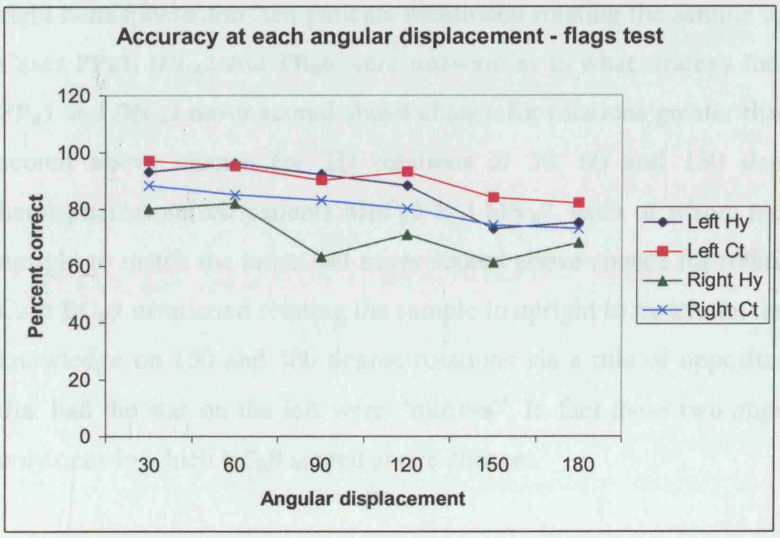
6.2.5.1 The Flags test

Table 6.5 summarises the results obtained for the flags test. Repeated measures ANCOVA was used to determine whether differences existed across groups for sets 1-3. Within subjects factor of set was used (3 levels pertaining to scores obtained on sets 1-3) and between subjects factors of Hemisphere (Right, Left) and Group (Control, Patient) were included. There was no evidence of an interaction between set, group and hemisphere, which did not confirm the prediction regarding right hemisphere performance. Evidence for a main effect of set was observed, which suggests that performance levels differed across the three sets (ANCOVA: $F(1,35) = 17.73$, $p < 0.001$). Follow up analysis revealed a significant linear trend ($F(1,35) = 21.77$, $p < 0.001$), showing increased error rates with increased angular rotation.

Table 6.5. Flags test scores - percent correct (mean +/- SEM).

	$HY_{L\ (N=12)}$	$CT_{L\ (N=11)}$	$HY_{R\ (N=10)}$	$CT_{R\ (N=8)}$	Study group $_{(N=41)}$
Set 1	96.67 (0.94)	93.64 (2.25)	85.5 (7.83)	89.38 (6.64)	91.7(2.4)
Range	90-100	80-100	20-100	45-100	20-100
Set 2	92.52 (2.5)	93.64 (4.27)	68 (6.96)	82.5 (8.35)	84.9 (3.08)
Range	70-100	55-100	40-100	35-100	35-100
Set 3	77.5 (7.75)	78.64 (9.34)	69.5 (9.59)	73.75 (11.41)	75.2 (4.53)
Range	30-100	10-100	20-100	20-100	10-100
Total score	88.89 (3.25)	88.64 (5.03)	74.33 (6.16)	67.13 (12.03)	83.9 (2.74)
Range	70-100	48-100	50-98	48-100	48-100

Figure 6:7. Mean percent correct at each angular displacement.



Accuracy was analysed with a repeated measures ANCOVA with within-subject factor rotation (6 levels pertaining to the 30 degree increments in the flags tests). There was no evidence of an interaction between rotation, group and hemisphere. It was therefore appropriate to look at main effects. There was a main effect of rotation (ANCOVA $F(1,35) = 11.57$, $p < 0.001$), illustrating different scores across groups for different angular displacement. Follow up analysis revealed a significant linear trend ($F(1,35) = 17$. $p < 0.001$), showing increased error rates with increased angular rotation.

6.2.5.2 *The Axis tests*

Table 6.6 summarises the results obtained for the axes test. Repeated measures ANCOVA was used to see if performance differed between percent correct on the Axis 1 and Axis 3 tests (to compare performance with a 3-D stimulus rotating around 1 v. 3 axes), and between percent correct on the Axis 1 and Flags tests (to compare performance rotating a 3-D stimulus v. a 2-D stimulus). There were no significant effects.

Table 6.6. Axis Test scores - percent correct (mean +/- SEM).

	$HY_{L\ (N=12)}$	$CT_{L\ (N=11)}$	$HY_{R\ (N=10)}$	$CT_{R\ (N=8)}$
Axis 1	66.15 (4.99)	76.08 (5.04)	65.69 (5.09)	76.35 (6.73)
Range	60-100	45-100	48-92	48-98
Axis 3	61.46 (5.7)	71.74 (5.1)	59.6 (4.46)	63.86 (6.32)
Range	35-96	52-98	46-96	46-98

6.2.5.3 *Metacognition*

Almost all participants were able to offer some form of explanation as to the cognitive strategy they used to ascertain the enantiomeric relationship between the target shape and the samples. 10 of 12 left hemispherectomised patients mentioned rotating the sample to upright to match the target. Cases **JS$_L$5** and **LO$_L$8** were unaware as to what strategy they used to complete the task, yet they scored above chance for 2D rotations between 30-120 degrees from upright. 7 of 10 right hemispherectomised patients mentioned rotating the sample to upright to match the target. Cases **PP$_R$1, DN$_R$2** and **TB$_R$6** were unaware as to what strategy they used to complete the task. **PP$_R$1** and **DN$_R$2** never scored above chance for rotations greater than 60 degrees, and **TB$_R$6** only scored above chance for 2D rotations at 30, 60 and 150 degrees. Of interest are right hemispherectomised patients **MM$_R$3** and **MS$_R$7**, each of whom mentioned rotating the sample upright to match the target but never scored above chance for rotations greater than 60 degrees. Case **BC$_R$9** mentioned rotating the sample to upright to match the target in addition to using tacit knowledge on 150 and 180 degree rotations via a rule of opposites, such that inverted stimuli that had the star on the left were "mirrors". In fact these two angular displacements were the only ones in which **BC$_R$9** scored above chance.

Similar patterns of results were found in controls, with the majority of participants mentioning rotating the sample to match the target. One participant mentioned a strategy but scored below chance (**RC$_{CL}$9**), others failed to mention a strategy and scored below chance (**GB$_{CR}$1** and

$GP_{CR}3$), and one participant failed to mention a strategy but scored above chance on 2D items (**$LB_{CL}4$**). Thus it seems there is no straightforward relationship between presence of metacognition and mastery of the flags task, though it is of note that none of the hemispherectomised patients and controls without relevant metacognition scored above chance on the axis tasks.

6.2.5.4 Age at seizure onset and task performance

Correlation analyses were run between age at seizure onset and results of each of the assessments reported above. For the left hemispherectomy group, age at seizure onset was positively correlated with scores on the Axis 1 test ($R = 0.837$, $p = 0.05$) and the Axis 2 test ($R = 0.711$, $p = .032$). There were no other significant correlations for the remaining study groups.

6.2.6 Discussion

The purpose of this section was to assess mental rotation abilities in hemispherectomised patients and their controls. The principal aims were to characterize the nature and extent of any impairment in this domain, whilst considering the relationships between task performance and variables such as side of hemispheric removal, presence of one versus two functional hemispheres, and age at onset of seizures.

6.2.6.1 The integrity of mental rotation in the isolated hemisphere

The results of the various assessments reported in this chapter provided convergent evidence that several left and right hemispherectomised patients were able to engage in mental rotation, with approximately two thirds of left hemispherectomised patients and a third of the right hemispherectomised patients being able to engage in complete mental rotation of 2 dimensional stimuli from 0-180 degrees. Approximately two thirds of control participants also attained this level of function. All groups found smaller rotations easier than larger rotations. Almost all participants were able to describe the internal mental transformation or strategy that was employed to compare samples to target stimuli, which suggests that metacognition, at least in terms of visual imagery, is available when conscious introspection is required in order to describe one's mental mechanics to an external observer. The broad spectrum of performance in both left and right hemispherectomised patients clarifies results from three previous case studies that document mental rotation abilities in hemispherectomised patients, one study reporting intact rotation after right hemispherectomy (Sergent and Villemure 1989), the other two reporting impaired rotation after left (Marriotti 1998) and right (Chiricozzi 2005) hemispherectomy. It seems these case studies represent a fraction of possible outcomes in hemispherectomised patients, hence the importance in using larger groups in order to gain an overall impression of the spectrum of performance in both left and right hemispherectomised groups.

Consideration of the pattern of performance in individual cases provides general support for the conclusions drawn above and also raises further interesting hints as to how these skills develop at the level of the individual child. The three tests used provide various measures of mental rotation ability that could be fractionated according to task complexity. The flags task enabled measurement of mental rotation when 2D objects are displaced 30-180 degrees within the z axis. Eight left hemispherectomised patients were able to establish the enantiomeric relationship of flag stimuli at all given angular displacements and explain their strategy, suggesting mastery of mental rotation of 2D objects. All left hemispherectomised patients were able to successfully engage in mental rotation of objects displaced between 30-120 degrees from upright. Of the four left hemispherectomised cases that had difficulty with 150 and 180 degree stimuli, **NW** $_{\mathbf{L}}$**9** and **KY**$_{\mathbf{L}}$**1** were able to perform left-right discrimination on inverted figures in the mental reorientation test (section 6.1), suggesting 180 degree rotation of *figures* was intact. It is of note that the remaining two left hemispherectomised patients that had difficulty with 150 and 180 degree stimuli without concomitant success on the mental reorientation task were the only two patients in the left hemispherectomy group without relevant metacognition. A similar pattern of success and limitation was found in the control group for these patients. Limitations began earlier in the right hemispherectomy group, with cases **PP**$_{\mathbf{R}}$**1**, **DN** $_{\mathbf{R}}$**2**, **MM** $_{\mathbf{R}}$**3** and **MS** $_{\mathbf{R}}$**7** being unsuccessful on stimuli rotated beyond 60 degrees and case **BC**$_{\mathbf{R}}$**9** was only successful on stimuli (150-180 degrees) that were amenable to application of his tacit knowledge to bypass rotation. Of the remaining five cases, **GB** $_{\mathbf{R}}$**4**, **SN** $_{\mathbf{R}}$**5**, **KD** $_{\mathbf{R}}$**8** and **EBK** $_{\mathbf{R}}$**10** were able to establish the enantiomeric relationship of flag stimuli at all given angular displacements and explain their strategy, suggesting mastery of mental rotation of 2D objects in the isolated left hemisphere. Six control participants for this patient group were able to successfully engage in mental rotation of objects displaced between 30-120 degrees from upright, of which five demonstrated mastery of mental rotation of 2D objects.

Collectively these results suggest that either isolated hemisphere can develop or sustain the ability to mentally rotate 2D objects in the z plane to establish enantiomeric relationships between target and sample, a skill that becomes evident between 6-8 years of age. The presence of relevant metacognition accords with this developmental level. Difficulties encountered for rotations at 150-180 degrees in both left and right hemispherectomised patients are at odds with studies of brain injured adults that report difficulties only for patients with right hemisphere lesions (Ditunno and Mann 1990, Ratcliff 1979), but accord with the finding that rotation impairment is not an all or none phenomenon.

The axis one task enabled measurement of mental rotation when 3D objects are displaced between 30-180 degrees in one of the three Cartesian axes. Four left (**EBT $_{L}$4, HW $_{L}$6, PD$_{L}$10, JL $_{L}$12**) and four right (**GB $_{R}$4, SN $_{R}$5, KD $_{R}$8, BC$_{R}$9**) hemispherectomised patients were successful on this task. All cases except **BC$_{R}$9** had demonstrated mastery of 2D rotation. These findings suggest that the isolated left or right hemisphere is able to use mental rotation to determine the enantiomeric relationship between 2 abstract geometric figures that may be separated by 30-330 degrees in any one of 3 Cartesian axes. The axis three task enabled measurement of mental rotation ability when 3D objects are displaced between 30-330 degrees in all three Cartesian axes. Four left (**KY$_{L}$1, HW $_{L}$6, PD$_{L}$10, JL $_{L}$12**) and two right (**GB $_{R}$4, SN $_{R}$5**) hemispherectomised patients were successful on this task, which demonstrates that the isolated left or right hemisphere is also able to ascertain enantiomeric relationships between 2 abstract geometric figures that have been rotated in a combination of the three axes.

Collectively, these results accord with studies that show both hemispheres are active during mental rotation, which in turn suggests that either hemisphere can mediate mental rotation (Vanrie 2002, Gauthier 2002). Although some authors have attributed bilateral activation to the employment of hemispheric specific strategies (Cook 1994, Alivisatos and Petrides 1996, Corballis 1997, Harris 2000), results from this study suggest that bihemispheric co-operation is not necessary for mental rotation of 2D or 3D shapes in any of the three Cartesian axes, though it is possible that such division of labour may occur in neurologically intact individuals.

Results from the mental rotation tests also shed some light on the presence or absence of relevant metacognition. Almost all participants were able to offer some form of explanation as to the mental strategy they used to ascertain the enantiomeric relationship between the target shape and the samples. Metacognition was not always synonymous with success on mental rotation tasks however, nor was lack of it always associated with failure. Cases **JS $_{L}$5** and **LO $_{L}$8** were unaware as to what strategy they used to complete the task, yet they scored above chance for 2D rotations between 30-120 degrees from upright. Right hemispherectomised patients **MM $_{R}$3** and **MS $_{R}$7**, each of whom mentioned rotating the sample upright to match the target but never scored above chance for rotations greater than 60 degrees. Case **BC$_{R}$9** mentioned rotating the sample to upright to match the target but success was only evident on trials where he utilised tacit knowledge. Thus it seems that strategies available for conscious introspection were not always implemented successfully when one considers test results, particularly the Axis tests. The study participants that lacked relevant metacognition never scored above chance on these two tests, though several cases (**PO $_{L}$2, RG $_{L}$3, CB $_{L}$7, TS $_{L}$11, EBK $_{R}$10**) that demonstrated metacognition and mastery of 2D rotation were below chance on these tasks. Thus it seems that metacognitive awareness is not always accompanied by cognitive competence in this domain, perhaps as a result of global cognitive impairment or dissociation between awareness of strategy and its successful implementation. The latter possibility is pertinent when considering case **EBK $_{R}$10**, with VIQ and PIQ within the average range, mastery of 2D rotation and metacognitive awareness but below chance performance on the axis tasks.

6.2.6.2 Comparison of left and right hemispherectomised patients

Collectively, results from the flags tests and Axis tests suggest that either isolated hemisphere is often capable of some degree of mental rotation. The degree of sophistication is highly variable across individuals, but a small number of cases are capable of resolving complex rotations in either a single Cartesian axis or indeed, a combination of all three. Presence of left and right hemispherectomised patients within this category suggests that the left hemisphere can mediate complex forms of mental rotation, which is at odds with studies demonstrating impaired rotation ability after focal right hemisphere lesions (section 6.2.1). It is possible that the damaged right hemisphere in these patients still attempts to mediate the task at hand, preventing the intact left hemisphere from demonstrating its competence. Similar arguments have been proposed for the presence of visual hemineglect (Plourde and Sperry 1984) and prosopagnosia (de Gelder 1998) after focal right hemisphere lesions. It is difficult to reconcile this with data from split brain studies in which the isolated left hemisphere appears to be incompetent at mental rotation until extensive practice ensues, though individual case data obtained in this study suggests that right hemispherectomised patients may be less competent than left hemispherectomised patients. Previous studies have argued that hemisphere specific differences emerge on 2D as opposed to 3D stimuli (Harris 2000) as a result of task complexity attenuating laterality profiles for 3D stimuli. The flags task data suggest that the isolated left hemisphere may have difficulty establishing mental rotation though it is acknowledged that **PP$_{R}$1, DN $_{R}$2** and **MM $_{R}$3** (aged between 8-12 years at test) may still develop such skills during adolescence, and there were no statistically significant group differences. Booth (2000) claims that in the context of large unilateral lesions sustained in childhood, subjects will employ neural resources in the intact hemisphere to mediate mental rotation, regardless of the side of the lesion. Results from the current study accord with this proposal, and support the notion that either hemisphere has the potential to develop rudimentary visuospatial function, with a small number of cases surpassing these basic expectations.

6.2.6.3 One versus two functional hemispheres

Scores were broadly similar between patient and control groups for each task, which suggests that mental rotation is affected similarly by generic reductions in cognitive function in the isolated hemisphere and in the presence of two cerebral hemispheres. These findings have important implications for previous studies (Cook 1994, Corballis 1997, Harris 2000) in which mental rotation was conceptualised as a bihemispheric process. It has been suggested that information passes from the right to the left hemisphere when difficult rotations are encountered in an attempt to attenuate the cognitive burden of the task (Harris 2000). This in turn, implies that mediation of difficult rotations could be particularly difficult for hemispherectomised patients. The results obtained in this study suggest that there appears to be a subset of individuals with general cognitive impairment that are fully capable of mental rotation, and the presence of one versus two functional hemispheres does not appear to be a significant factor in performance. Similarly, there is a subset of individuals who encounter difficulties with all but the smallest of rotations, with no clear distinction between the presence of one versus two functional hemispheres.

6.2.6.4 Age at onset of seizures and task performance

Correlational analysis revealed a positive relationship between age at seizure onset and task performance in the left hemispherectomy group, which suggests that patients with later onset of seizures in the left hemisphere may encounter a particular advantage in the development of mental rotation skills as compared to patients with earlier onset of left hemisphere seizures or patients with right hemisphere disease. This implies that as development proceeds, mental rotation functions within the right hemisphere become increasingly impervious to the effects of reorganisation of function as a consequence of cerebral injury, which accords with the crowding hypothesis and theories of interactive specialisation. These possibilities remain to be substantiated with larger sample sizes.

Overall, the results suggest that the isolated left or right hemisphere can engage in mental rotation of 2D and 3D objects displaced between 30-330 degrees along any of the three Cartesian axes in order to establish enantiomeric relationships, which suggests that unilateral cerebral injuries sustained in childhood may have different consequences from those sustained in adulthood, with the latter group demonstrating side specific deficits. It must be acknowledged however that mental rotation involving large angular displacements or 3D objects rotated in the three axes may remain elusive in some cases, suggesting that mental rotation is not an all or none phenomenon. Lack of differences between patients and controls imply that in the context of cognitive impairment, one hemisphere is no less efficient than two cerebral hemispheres at performing mental rotations, which poses problems for the proposal that mental rotation is a bihemispheric process. Further study would involve analysis of performance using alphanumeric and familiar objects within the three Cartesian axes to see if stimuli specific effects or impaired performance in a particular axis affected results.

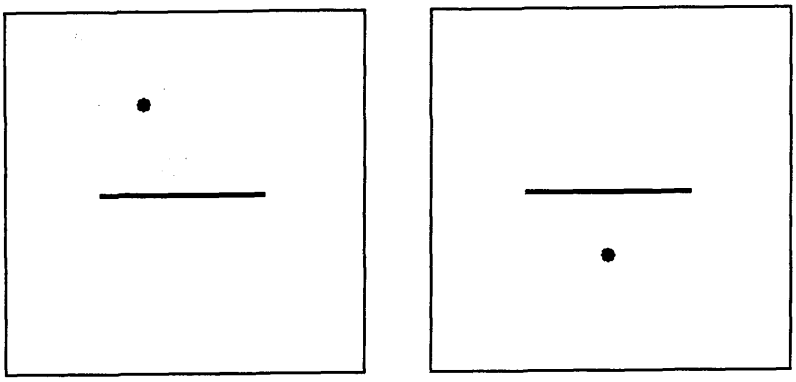
6.3 Judgements in metric and categorical space

6.3.1 Introduction

In addition to utilising ego and allocentric reference frames to encode spatial relations between self and objects in the environment, spatial relationships may also be represented by categorical and metric forms of reference. Categorical relations refer to the perception and expression of basic relational information, those in which the spatial relationship between items can be qualitatively described by discrete, unambiguous categories (e.g. above, below, to the left etc). These terms extract the essentials of spatial relations by discarding non crucial specifics, which in turn affords rapid verbal communication of meaningful information. This form of description of spatial relations has practical application in situations when immediate decisions regarding action based on spatial locations of objects must be made or communicated to others.

Metric relations refer to the perception and expression of precise locations of objects or their components in metric units, thus yielding exact distances along a continuum of values, as opposed to the binary nature of categorical labels. This type of spatial representation is useful when navigating in the environment or when engaging in skilled manipulation of objects. A variety of stimuli have been used to elicit categorical and metric judgements, and all share the advantage of using the same stimuli for each condition. A popular example of a stimulus set is the horizontal bar and small dot either above or below it (Figure 6.8). Categorical judgements pertain to whether the dot is above or below the line, whereas metric judgements require subjects to decide if the dot is within a specified distance of the line.

Figure 6:8. Typical stimuli used in categorical and metric processing experiments.



Categorical and metric processing are often presumed to be independent domains as computing categorical spatial relations does not provide information about metric spatial relations and vice versa (Kosslyn 1987, 1989), although there is some evidence of interaction between the two. For example, some studies have shown that metric information can affect categorical processing, with smaller distances resulting in slower categorical decisions (Sergent, 1991; see also Wilkinson & Donnelly, 1999). This suggests that categorical spatial information is contained within metric spatial information as a method of constraining and forming more precise spatial metrics, and thus forms an early stage in metric processing (Sergent, 1991). Another study has shown that categorical information primes precise metric judgements though the reverse is not true (Niebauer, 2001). This results suggests that, while categorical and metric systems do interact in terms of categorical information being used to form more precise metric judgments, metric information is not used to formulate categorical decisions (Niebauer (2001)

6.3.1.1 The anatomy of metric and categorical spatial processing

Results from the behavioural studies described above have important implications when attempting to define the anatomical substrates of categorical and metric processing. These two modes of processing are commonly believed to be qualitatively different and as such, employ different neural substrates. Kosslyn (1987) proposed that the left hemisphere was preferentially involved in/makes more effective use of categorical processing, whereas the right hemisphere was preferentially involved in metric processing. The notion of hemispheric differences in processing categorical and metric spatial relations has been explained via neuronal properties and attentional biases within the left and right hemispheres. Kosslyn (1987) and Banich (1999) suggest that lateralisation of these two frames of reference may derive from differential processing of receptive field output in the later stages of cognitive processing, a proposal that has been suggested previously (Sergent 1985). The idea of categorical processing being a left hemisphere specialisation is based on the idea that processing in the left hemisphere is mostly based on input from neurons with small, discrete receptive fields. Categorical decisions could thus be executed rapidly in a system with small discrete receptive fields. The nature of the categorisation process was conceptualised by Kosslyn (1987). He postulates that receptive fields for surrounding space are grouped into "bins" that have specific categorical relations relative to the object of regard. In this manner, a second object may be compared to the object of regard by considering the relation between this object and the bin in which the second object is situated.

Conversely, metric processing in the right hemisphere is based on computations via specific activation profiles extracted from combined activity of neurons with larger, overlapping receptive fields. The idea that hemispheric specialisation for computing different types of spatial relations is based on receptive field properties is consistent with findings of differential hemispheric sensitivity to high and low spatial frequencies (Christman 1991, Peyrin et al 2003). Kosslyn (1994) adds that differences in attentional biases in the left and right hemisphere may also contribute to differences in spatial processing, whereby large and small regions of space cannot be attended to simultaneously, hence different types of attentional bias are needed according to the magnitude of the to be attended field. In accordance with receptive field properties mentioned earlier, the left hemisphere is viewed as having an attentional bias towards processing information from small areas of space, whereas the right hemisphere attends to larger areas of space. Thus it seems that although the two hemispheres receive the same visual information, they may not utilise visual input to the same degree, or perform all computations with equal efficacy. This is supported by studies illustrating differential hemispheric sensitivity to global and local aspects of visual stimuli (Fink 1996, Moses et al 2002). Whilst Kosslyn's hypothesis is appealing, there is little evidence from electrophysiological recording studies to support the notion of hemispheric asymmetry for cellular receptive fields. In fact, available evidence from feline studies appears to support the opposite pattern of larger receptive fields in visual cortical cells of the left hemisphere (Gabibov 1992, 1993). Despite this shortcoming, Kosslyn's hypothesis blends well with evidence relating to hemispheric asymmetries for processing different spatial frequencies, and asymmetries relating to categorical and metric processing.

Studies that focus on the functional dissociation between the hemispheres for categorical and metric processing have mostly used visual half field paradigms with neurologically intact adults. Results are generally encouraging from these tasks, and provide empirical support for Kosslyn's model, which suggests that responses to metric trials are faster and more accurate when presented to the LVF, supporting the notion of right hemispheric dominance in both adults (Hellige and Michimata 1989, Michimata 1997, Kosslyn 1989, Laeng and Peters 1995, David and Cutting 1992, Niebauer and Christman 1998, Servos and Peters 1990) and children (Koenig 1990). Whilst support for RVF advantages for categorical stimuli has been somewhat weaker (e.g., Sergent, 1991), some studies have indeed obtained robust RVF advantages (Hellige and Michimata 1989, Koenig 1990, Michimata 1997, Parrot 1999, Okubo 2002, 2004).

It is possible that task difficulty may serve as a potential confounding factor when investigating hemispheric differences in categorical and metric processing (Bruyer 1997, Okubo 2002) though Kosslyn (1989) argued against this possibility. As categorical judgements are usually based on a conceptually distinct binary choice process, it is possible that these judgments are indeed easier than judgments in metric space, which are based on response selection from an infinite scale, whose intervals are less sharply defined in conceptual terms. Indeed, categorical judgements are made faster and/or more easily according to some studies (Bruyer 1997, Okubo 2002). Parrot (1999) suggests that left hemispheric advantages were observed when tasks were easy, and right hemispheric advantage for metric processing became stronger for difficult tasks. She suggests that lateralisation may reflect a left hemisphere advantage for processing easy spatial stimuli and a right hemisphere advantage for processing relatively difficult stimuli, based on the right hemisphere advantage being evident only for very difficult metric judgments. This accords with results from Wilkinson and Donelly (1999), whereby reduced LVF advantage for longer stimulus exposures may reflect a reduction of task difficulty. Slotnick (2001) also suggests that task difficulty emphasises hemispheric differences in categorical and metric spatial processing. These observations interact with the debate focused on whether categorical and metric processing are orthogonal phenomena, as Parrot concludes that easy stimuli may be processed categorically, whilst more difficult stimuli tend to engage metric spatial processing.

Visual half field studies in neurologically intact subjects have provided moderate support for Kosslyn's hypothesis. Neuroimaging studies and patient investigations have provided converging evidence for lateralisation of categorical and metric processing, though support is by no means complete. The posterior parietal lobes appear to be particularly important in categorical and metric processing, in accordance with their established role in spatial cognition. Kosslyn's (1998) PET study of simple categorical and metric judgements provides general support, showing that in addition to a common pool of fronto-parietal activation, distinct networks were involved in computing the two types of relation. Left hemisphere activation was evident during the categorical task and right hemisphere activation was relatively strong in the metric task. Interestingly, there was only partial support for lateralised parietal involvement in this task, with right SPL and precuneus being more strongly activated in metric processing tasks, but left frontal regions being differentially active in categorical tasks. This was interpreted as temporal constraints of PET failing to demonstrate the relatively rapid, automatic processing involved in categorical judgements, an interpretation supported by results from fMRI showing the expected pattern of parietal lateralisation (Baciu 1999, Trojano 2002)

Studies with clinical populations provide further evidence for and against hemispheric specialisation of categorical and metric processing and the importance of the parietal lobes. Sergent's (1991) study of 3 commisurotomised patients suggests that both hemispheres are able to perform above chance in both types of task, and there was no interaction between type of task and visual half field, suggesting the performance of each hemisphere was similar for computing categorical and metric spatial relations. In a more recent study using subjects with one hemisphere temporarily deactivated by sodium amobarbital, Slotnick (2001) found that increasing task difficulty led to a left hemisphere advantage for categorical processing and a right hemisphere advantage for metric processing. Studies using patients with unilateral lesions have been generally supportive of Kosslyn's hypothesis. Laeng (1994) found that patients with left parietal lesions made more errors on a categorical judgement task, whereas patients with right parietal lesions made more errors on a metric judgement task. It is of note that lesions of the left angular gyrus are associated with impaired left-right discrimination as mentioned in section 6.1.1, which is an example of categorical spatial processing.

There are no comparisons of categorical and metric spatial processing in hemispherectomised patients to date, and there are just 3 studies that document performance in one of these domains. In her study of two left hemispherectomised patients, Ogden (1989) administered a basic drawing test that involved plotting categorical spatial relations, and performance was intact in both cases. Marriotti (1998) administered two tests of metric spatial processing to left hemispherectomised patient MP, who demonstrated impaired performance on both tasks. Chiricozzi (2005) administered the same metric processing tasks to right hemispherectomised patient GT, who obtained good scores in both tasks. Thus it remains to be seen whether categorical and metric processing can be mediated with equal efficiency in an isolated left and right hemisphere in these patients. Current findings must be substantiated using a larger group of patients, and will provide an interesting perspective on the debate surrounding cerebral laterality of function in categorical and metric processing.

6.3.1.2 The development of metric and categorical spatial processing

There is a paucity of literature that directly addresses the developmental trajectory of categorical and metric spatial processing. Koenig (1990) tested children aged 5:0 and 7:0 on a categorical-metric spatial processing task involving above/below and near/far judgments of simple line and dot stimuli. A divided visual field paradigm was used to assess hemispheric differences. Scores for categorical processing were higher than metric processing. In both groups of children, a left visual field advantage was found for metric judgments, whereas a right visual field advantage was found for categorical judgments, resembling the pattern found in adults. It is of note however, that hemifield advantages were only apparent in the early blocks of trials, suggesting that with practice, both hemispheres were capable of mediating categorical and metric judgements.

Extrapolation to the development of distance estimation and spatial category learning suggest that categorical processing emerges before metric processing, with basic categorical reference terms being acquired between 4-6 years of age. As mentioned in section 6.1, different sets of referential axes appear at different stages, with up-down, and front-back being in place by 4 years of age, and correct use of left-right emerging between 6-12 years of age. The child's spatial environment can thus be fractionated into distinct sub locations by using a small collection of reference terms that will effectively communicate the whereabouts of a particular object with respect to self and others. Distance estimation and use of a metric reference framework is mastered between 9-10 years of age (Temple 2000). There is relatively little use for this frame in everyday life unless measuring or estimating whether something is "near" or "far", which is arguably at the interface of metric and categorical processing. The majority of research focusing on distance estimation involves experimental paradigms that are markedly different from those used to investigate categorical and metric processing. Subjects often walk along a predefined route and are asked to judge the route distance (Fabricius 1993) and the relative distance of objects that were placed along the route (Herman 1983). Further investigation is required to understand the maturational trajectory of categorical and metric processing in the developing brain, including possible effects of cerebral injuries sustained in childhood. Using a bar and dot task similar to Koenig (1990), Schatz (2004) found that categorical processing was preserved relative to metric processing regardless of side of injury in children that had sustained unilateral cerebral infarcts. This implies that in the context of early brain injury, there may be a predisposition to adopt the simplest form of conceptualising spatial relationships, i.e. the binary categorical system.

6.3.2 Aims and predictions

The principal aims of this neuropsychological study of categorical and metric spatial processing in hemispherectomised patients were (1) to characterize the nature and extent of any impairment in this domain; (2) to determine the relationship between side of hemispheric injury and task performance; (3) to determine whether categorical and metric processing is more efficient when mediated by two functional cerebral hemispheres (4) to address the issue of age at clinical onset of pathology/seizures on task performance.

Between groups comparisons of neuropsychological data from the patient and control groups were carried out. The predictions were as follows:

- Left hemispherectomised patients would be more likely to obtain lower scores on the categorical task than right hemispherectomised patients and controls.
- Right hemispherectomised patients would be more likely to obtain lower scores on metric tasks than left hemispherectomised patients and controls.
- Age at onset of seizures will be positively correlated with task performance in left hemispherectomised patients as visuospatial functions in the right hemisphere become increasingly impervious to the effects of crowding.
- become increasingly impervious to the effects of crowding.

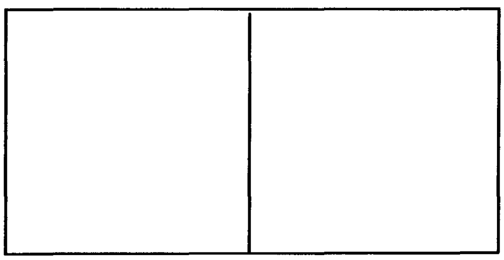
6.3.3 Methods

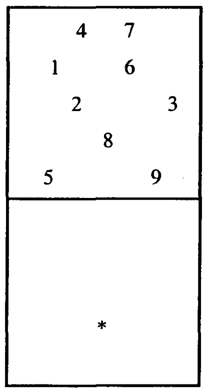
6.3.3.1 The Visual Object and Space Perception battery

The position discrimination and number location subtests of the Visual Object and Space perception Battery (Warrington and James 1991) were administered to provide a measure of metric spatial processing. The position discrimination task consists of 20 stimulus cards, each depicting 2 adjacent horizontal white squares. There is a 5mm black dot inside each square. Subjects are required to decide which of the two boxes has a dot placed exactly in the centre. The distractor box has a black dot displaced above, below, to the left or to the right of the centre. Subjects score 1 point for each correct answer, producing a maximum of 20 points. The cut off level for the task is 18/20. This test has previously demonstrated right hemisphere associated deficits in adult patients (Warrington and James 1991). Chance level was set at 50 percent for this task (two possible responses).

The number location task consists of 10 stimulus cards, each depicting 2 squares, one above the other with a small gap between them. The top square contains randomly placed numbers (1-9), whereas the bottom square contains a single black dot. The position of the dot corresponds with the spatial location of one of the numbers in the top square, and subjects are required to name the number that corresponds with the location of the dot. Subjects score 1 point for each correct answer, producing a maximum of 10 points. The cut off level of the task is 7/10. This test has previously demonstrated right hemisphere associated deficits in adult patients (Warrington and Taylor 1991).

Figure 6:9. Examples from the position discrimination and number location subtest of the VOSP





6.3.3.2 *Spot the dot test*

The Spot the Dot Test was designed to provide a measure of categorical and metric processing using a single stimulus set that resembles those used in most experimental tasks. Each trial consisted of 2 adjacent horizontal white squares measuring 60mm x 60mm (see figure 6.8). The squares were presented on a 15" laptop computer monitor. There was a black horizontal bar measuring 30mm in length placed in the centre of each square and a black circular dot measuring 2mm in diameter in each square. On a given trial, the dot could appear in one of 18 positions relative to the bar (9 above and 9 below, each position separated by 4mm). In the categorical version of the task, individuals judged which box contained a dot that was above the bar. In the metric task, individuals decided which dot was closest to the bar. Responses were made on the laptop keyboard by pressing the Z key to select the left box or the M key to select the right box. The space bar was used if the 2 boxes contained identical stimuli. Each of the 18 dot positions was presented 8 times (4 same trials, 4 different trials) in the categorical task, producing 144 trials. Subjects scored 1 point for each correct answer, producing a maximum of 144 points. In the metric task, each of the 18 dot positions was presented 12 times (4 same trials, 4 different – same level (both above or both below the bar) trials, 4 different – different level (one above and one below) trials), yielding a total of 216 trials. Subjects score 1 point for each correct answer, producing a maximum of 216 points. Chance level was set at 40 percent for the categorical and metric tasks (three possible responses). Responses were measured according to accuracy rather than reaction time (RT). Several studies confirm that accuracy is an equivalent or superior dependent variable in categorical metric tasks (Bruyer 1997, Slotnick 2001), and the obvious motor constraints in the hemispherectomy population render RT a highly unstable variable.

6.3.4 Analyses

Analyses were carried out as described in chapter 2, section 2.2.4. Age at test and PIQ were used as covariates in ANCOVA models unless otherwise stated.

6.3.5 Results

6.3.5.1 The Visual Object and Space Perception Battery

Table 6.7 summarises the results obtained for the VOSP subtests. Statistical analysis using ANCOVA revealed no differences between groups in terms of total scores obtained for either of the VOSP subtests. Repeated measures ANCOVA was computed for the position discrimination test using within subjects factor of direction (2 levels pertaining to scores obtained for left and right sided targets) and between subject factors of Hemisphere (Right, Left) and Group (Control, Patient). There were no interactions or main effects, suggesting that scores for the left and right squares were not significantly different for patients and controls, and thus hemianopia does not appear to affect performance.

Repeated measures ANCOVA was also used to see if scores differed between the two metric processing tests of the VOSP using the within subjects factor of test (2 levels pertaining to scores for each test) and between subject factors of Hemisphere (Right, Left) and Group (Control, Patient). Evidence for a main effect of test was observed (ANCOVA: $F(1,34) = 21.21$, $p < 0.001$), suggesting that scores for the two metric processing tests were significantly different across groups, with number location being more difficult than position discrimination.

Chi squared tests did not reveal any significant differences between groups with respect to the number of cases below the cut off score in either of the VOSP subtests.

Table 6.7. VOSP subtest scores - percent correct (mean +/- SEM).

	$HY_{L\ (N=12)}$	$CT_{L\ (N=11)}$	$HY_{R\ (N=10)}$	$CT_{R\ (N=8)}$
Position discrimination	80.83 (4.12)	85 (4.05)	81 (4.27)	83.75 (6.73)
Range	60-100	65-100	55-95	55-100
Patients below cut off 18/20	8	4	6	4
Left squares	83.3 (4.32)	81.82 (6.15)	76.67 (5.1)	82.5 (8.81)
Right squares	81.67 (5.75)	88.18(5.36)	82.22 (5.21)	85 (7.79)
Number location	50 (9.77)	61.82 (9.98)	56 (11.08)	66.25 (14.63)
Range	0-100	0-100	0-90	10-100
Patients below cut off 7/10	7	7	5	4

6.3.5.2 *Spot the dot test*

Table 6.8 Summarises the results obtained for the spot the dot test (STD). Statistical analysis using ANCOVA was carried out for total scores obtained on the categorical and metric subtests using between subject factors of Hemisphere (Right, Left) and Group (Control, Patient). Evidence for a main effect of group was observed on the categorical task (ANCOVA: $F(1,34) = 15.455$, $p < 0.001$), with patients obtaining lower scores than controls. Repeated measures ANCOVA was computed for the categorical and metric subtests using within subjects factor of test (metric, categorical) and between subject factors of Hemisphere (Right, Left) and Group (Control, Patient). Evidence for a main effect of test was observed (ANCOVA $F(1,34) = 36.17$, $p < 0.001$), suggesting that scores on the categorical test were higher than scores on the metric test across groups. Weak evidence for a main effect of group was also observed (ANCOVA $F(1,34) = 3.93$, $p = 0.056$), suggesting that differences between test scores may have different profiles in patients and controls.

Table 6.8. Spot the dot test scores - percent correct (mean +/- SEM).

	$HY_{L\ (N=12)}$	$CT_{L\ (N=11)}$	$HY_{R\ (N=10)}$	$CT_{R\ (N=8)}$
Categorical	90.5 (1.08)	93.12 (0.36)	86.6 (1.85)	93.49 (0.47)
Range	84-94	91-94	78-94	91-95
Metric	73.53 (4.17)	81.27 (2.89)	79.12 (3.85)	82.47 (3.78)
Range	44-92	67-94	57-93	59-94

Repeated measures ANCOVA was computed to see if differences existed between scores for the metric component of this test and the number location test of the VOSP. Within subjects factor of test (2 levels pertaining to scores for each test) was used. Evidence for a main effect of test was observed (ANCOVA: $F(1,34) = 22.71$, $p < 0.001$), suggesting that scores on the metric STD test were higher than scores on the number location test across groups.

6.3.5.3 Age at clinical onset of pathology and seizure onset

Correlation analyses were run between age at seizure onset and results of each of the assessments reported above. For the left hemispherectomy group, age at seizure onset was positively correlated with scores on the metric subtest of the spot the dot test ($R = 0.794$, $p = 0.011$) and number location subtest of the VOSP ($R = 0.738$, $p = 0.023$). There were no other significant correlations for the remaining study groups

6.3.6 Discussion

The purpose of this section was to assess categorical and metric spatial processing abilities in hemispherectomised patients. The principal aims were to characterize the nature and extent of any impairment in this domain, whilst considering the relationships between task performance and variables such as side of hemispheric removal, presence of one versus two functional hemispheres, and age at onset of seizures.

6.3.6.1 Functional integrity of categorical and metric processing

The results of the various assessments reported in this chapter provided evidence that the isolated left or right hemisphere is able to engage in both categorical and metric spatial processing. Within the metric processing tasks, scores on position discrimination and spot the dot tests were higher than scores on the number location test across groups, demonstrating that tasks of different levels of complexity were included in the study. This is important when one considers previous controversies in studies attempting to examine laterality effects in metric and categorical processing using stimuli that were considered very easy or very difficult (Rybash 1992, Bruyer 1997, Parrot 1999, Slotnick 2001).

Results from the categorical processing subtest of the spot the dot (STD) test reveal that the isolated left and right hemispheres are able to perceive and accurately describe categorical spatial relationships using the above-below axis, a skill that is usually evident by 6 years of age. All participants were able to successfully determine whether the dots were above or below the line, and to respond appropriately, with scores above chance levels on this task. All groups found categorical processing easier than metric processing, with lower scores for the latter group of tests. The integrity of "above-below" categorical processing in all patients and controls may be compared with results in section 6.1 regarding left-right discrimination. It appears that either isolated hemisphere may compute categorical spatial relations within an egocentric frame of reference to specify vertical and horizontal locations such as above, below, left and right in order to communicate spatial location to another observer. This accords with findings from a previous study of categorical and metric processing in children with unilateral brain injury

(Schatz 2004) that demonstrated intact categorical relative to metric processing regardless of side of hemispheric injury.

When considering scores from metric processing tasks, performances on the position discrimination and metric STD tests were comparable, and superior to scores on the number location test in all groups. Almost all hemispherectomised patients and controls obtained scores above chance on the metric STD test, with just two left (**PO $_L$2, NW $_L$9**) and 1 right (**PP$_R$1**) hemispherectomised cases scoring below chance. The cut off score for the position discrimination task as stipulated in the manual was very high (90 %), yet 4 left (**KY$_L$1, HW $_L$6, PD$_L$10, JL $_L$12**) and 4 right (**MM $_R$3, SN $_R$5, MS $_R$7, KD $_R$8**) hemispherectomised cases obtained scores at or above this level. These results suggest that the isolated left and right hemispheres are able to make relatively simple near/far judgments in metric space, and to respond appropriately. These results accord with studies that claim the either hemisphere is able to engage in simple spatial judgements using categorical and metric frameworks (Parrot 1999, Wilkinson 1999, Slotnick 2001).

The limitations of metric processing are reflected in performance on the number location test. Scores on this test were lower than performance on the other metric processing tasks across groups. The cut off for this test was lower than the position discrimination test (70%), with 5 left (**EBT $_L$4, HW $_L$6, PD $_L$10, TS $_L$11, JL $_L$12**) and 5 right (**GB $_R$4, SN $_R$5, KD $_R$8, BC$_R$9, EBK $_R$10**) cases obtaining scores at or above the cut off level, therefore attaining a developmental level of at least 10 years of age with respect to metric spatial processing. A common tendency in patients and controls obtaining lower scores was to select the number that was most physically proximal to the dot, and in an approximate mirror image location. Thus if the dot was in the left half of the square, the number closest to the bottom of the number square was selected that was in a location that approximated the dot in a left-right but not an above-below axis (see figure 6.9 – number 5 would be erroneously selected). It is possible that utilization of 2 different axes to compute the metric relationship between the dot and its corresponding number was particularly difficult, resulting in a single horizontal metric axis being used, but this seems unlikely, as although the position discrimination task only required computation within one axis to obtain a correct response, with the displaced dot being only above, below, to the left or to the right, a substantial number of trials on the metric SDT did in fact require computation in both horizontal and vertical axes to produce the correct response. Dots that were the same vertical distance from the bar were often displaced horizontally, and were sometimes on the opposite side of the bar, requiring an extra calculation after the vertical distances had been verified before a response could be given. It therefore seems likely that the presence of multiple distractors disrupted computation of metric spatial relationships between the 2 targets in the number location task. This accords with the tendency to select the most proximal "mirror image", resulting in repeated selection of numbers from the bottom of the number square.

6.3.6.2 Comparison of left and right hemispherectomised patients

Results from patients that did obtain scores above chance on categorical and metric processing tasks were encouraging, and provide evidence that the isolated left or right hemisphere is able to utilise both of these spatial reference frames to compute precise locations of objects amongst multiple spatial distractors. There are no apparent differences between mean scores obtained by left and right hemispherectomy groups in any of the assessments included in this section, and a number of cases in both groups demonstrated mastery of categorical and metric processing in these assessments. These results are at odds with studies claiming that hemispheric differences exist with regards to categorical and metric processing in children and adults (see section 6.3.1.). Previous studies have drawn upon logical and empirical evidence to suggest relative specialisation of the left and right hemispheres of categorical and metric spatial processing respectively. It is difficult to reconcile the proposal that the anatomical layout of each hemisphere with respect to neuronal receptive fields and tract connectivity forms the basis of selective aptitude for these two methods of spatial computation. Left hemispherectomised patients may not develop competency on complex metric spatial processing tasks, despite an intact right hemisphere, which accords with the case study reported by Marriotti (1998). Similarly, right hemispherectomised patients may develop competency on these tasks with an isolated left hemisphere, which accords with results from Chiricozzi (2005) and Sergent and Villemure (1989). Although one cannot rule out the possibility of altered intrahemispheric connectivity in the face of contralateral cerebral injury, it is of note that right hemispherectomised patients with onset of pathology after five years of age may still develop competence on complex metric processing tasks. Results from this study suggest there is a degree of hemispheric equipotentiality during childhood regarding development of categorical and metric processing. Following unilateral cerebral injury, the developing brain will acquire skills in both types of spatial reference frame, despite global reduction in cognitive function and reduction of available neural substrate. Relative competence on categorical tasks regardless of side of injury accords with results from Schatz (2004), and supports the notion that in the context of early brain injury, there may be a predisposition to adopt the simplest form of conceptualising spatial relationships, i.e. the binary categorical system.

It is acknowledged that task complexity effects could have masked possible differences. The categorical task was particularly easy, and the position discrimination and metric spot the dot tests were completed efficiently by most participants. It is possible these tasks were not of sufficient complexity to reveal deficits in the right hemispherectomy group. The number location test was a more complex measure of metric processing however, yet half of the right hemispherectomised patients obtained scores above the cut off level. This task is regarded as the most complex spatial task of the VOSP battery, and is not mastered until 9-10 years of age (Temple 2000). It is encouraging that several cases were able to complete this test efficiently without a right hemisphere, which challenges previous literature that suggests that this test is acutely sensitive to right hemisphere damage (Warrington and Taylor 1991) though conclusions were based on adult patients. It seems that in the context of unilateral injuries sustained in childhood, categorical spatial referencing can develop or is sustained, perhaps due to its relative simplicity. Simple metric spatial judgements are also evident, which accords with studies that claim either hemisphere can mediate simple metric and categorical judgements (Sergent 1991), with several patients developing beyond these levels of competency.

6.3.6.3 One versus two functional hemispheres

Scores were broadly similar between patient and control groups for all tasks, which suggests that these spatial reference frames are affected similarly by generic reductions in cognitive function in the isolated hemisphere and in the presence of two cerebral hemispheres. The similarity between patient and control groups calls into question previous suggestions that hemispheric co-operation is necessary for this mode of spatial processing (Parrot 1999), though it is acknowledged that such studies are few in comparison to the number of testimonials in support of categorical and metric processing being confined to different hemispheres.

6.3.6.4 Age at seizure onset and task performance

Correlational analysis suggests that as development proceeds, metric spatial processing in the right hemisphere may become increasingly resistant to the effects of cerebral injury. This accords with theories of hemispheric crowding, and implies that these spatial skills are of sufficient necessity to remain consolidated when seizures occur later in childhood, although they may never reach maturity if seizure onset occurs during infancy or early childhood. These results remain speculative and must be substantiated with larger sample sizes.

Collectively, the results obtained in this section suggest that when unilateral cerebral injuries have been sustained during childhood, categorical and metric frames of reference can develop within the same hemisphere. The contributions of the left and right hemisphere to categorical and metric processing may thus not be as sharply distinct as Kosslyn's hypothesis suggests. Results were not suggestive of a relationship between side of hemispheric injury and task performance, with no significant differences between left and right hemispherectomy groups on any of the assessment measures in this section. These findings are at odds with previous literature that suggests preferential roles for the each hemisphere in categorical and metric processing, though task complexity effects may have influenced results. Scores were broadly similar between patient and control groups for metric processing tasks, which suggests that this spatial reference frame is affected similarly by generic reductions in cognitive function in the isolated hemisphere and in the presence of two cerebral hemispheres. The correlations observed between age at seizure onset and task performance in the left hemispherectomised patients suggest that as development proceeds, metric spatial processing in the right hemisphere may become increasingly resistant to the effects of cerebral injury.

7 Construction

7.1 Introduction

Constructional performance involves planning and executing a sequence of motor responses that will enable manual reproduction of a visual stimulus. The attended visual stimulus is perceived, encoded and translated into spatial co-ordinates, which can be used to generate a sequence of motor responses that will enable reproduction of the stimulus. Reproduction from memory is also possible via generation of visual images that lend themselves to further elaboration within the spatial co-ordinate system. Constructional function is typically assessed using tasks that require drawing or assembling an object, either from memory or by viewing a picture or model of the to-be-constructed stimulus. The aim of this chapter was to investigate the integrity of constructional abilities in hemispherectomised patients. Drawing tests were selected as measures of constructional function for this study, as block construction and model assembly paradigms generally employ the use of two hands, which would create further difficulties for the hemispherectomised patients. Thus, the introduction will focus on reviewing information on drawing abilities.

7.1.1 The anatomy of constructional function

7.1.1.1 The Parieto-Frontal Circuit

Given the complexity of the process of construction, it is unsurprising that several different brain regions appear to be involved. The majority of evidence from neuroimaging studies and from patients with focal cerebral lesions suggests that parieto-frontal circuits may be particularly important for constructional function, which accords with the observation that constructional function has both cognitive and motor components. Replicating prior work with older imaging methods, (e.g., Roland 1980), two recent fMRI (Ino, 2003; Makuuchi, 2003) studies of drawing movements have demonstrated bilateral parietal activation (particularly within the SPL and the depths of the intraparietal sulcus) and the left precentral gyrus. These studies suggest that the role of the parietal lobes in construction is likely to provide a unified representation of space via realignment of the spatial co-ordinates of the internal construct generated from direct percepts or memory to an internally defined system of spatial co-ordinates. The frontal motor components of the activation pattern are thought to reflect the construction of movement sequences based on output from the internally defined spatial co-ordinate system to effect goal directed actions. Kinematic analysis of drawing movements (Dounskaia et al 2002, Verschueren 1999) reveal that drawing is a multijoint movement that involves co-ordinated sequential movements of the muscles and joints of the shoulder, elbow and wrist, with progressively fine attunement of the end point movement that culminates in small adjustments in the fingers to produce the precise drawing movement required. Supplementary motor areas are active during programming and execution of movement sequences (Ino et al 2003). These regions are thought to generate motor programmes that make use of semantic information and are thus necessary for skilled voluntary action (Devinsky 1995). The premotor cortex is also associated with acquisition of new motor programmes or modulation of existing motor programmes based on visual input (van Mier et al 2004, Chouinard 2006), and the primary motor cortex is the executive centre for voluntary movements of the hand and arm (Makuuchi 2003). FMRI studies have also reported activation in other areas including the cerebellum and inferior temporal sulci. (Devinsky 1995; Ino, 2003; Makuuchi, 2003). The cerebellar activity may reflect its role in temporal sequencing of motor activity and mediating proprioceptive feedback. Activation of the inferior temporal sulcus may subserve constructional function by providing knowledge of shapes or parts of objects, as the intention to draw may trigger automatic or implicit retrieval of object shape as an aid to reproducing the object (Makuuchi et al 2003). This receives support from the presence of intellectual as opposed to visual realism in drawings (Freeman 1980), as one tends to draw familiar objects based on semantic knowledge as opposed to unbiased observation.

Collectively, these findings imply that there is a large bilateral network of brain regions involved in construction, but that different regions within this network subserve specific aspects of construction, and therefore lesions in different regions may result in different sources of constructional impairments. Parietal lesions may disrupt the internal spatial representation system necessary to guide movements, whereas frontal lesions may prevent the co-ordinate system being utilised for the generation of movement sequences. The question remains as to whether different outcomes are apparent following left and right hemisphere lesions.

7.1.1.2 Roles of the Left v. Right Hemisphere.

Deficits in constructional function have been demonstrated in adults with left-sided focal cerebral lesions. The term constructional apraxia (CA) was proposed by Kleist in 1934, and referred to an acquired deficit in the ability to reproduce spatial relationships in the context of intact motor function. Patients typically demonstrate impaired performance on measures of block construction and drawing (Smith and Gilchrist 2005). Kleist originally attributed CA to left parietal lesions, which received further support when CA was described as a component of Gerstmann's syndrome, which had also been attributed to left parietal lobe damage. A substantial body of literature confirms that CA is not exclusively related to left parietal lobe damage, in fact it can be related to posterior lesions in either hemisphere (Gainotti 1985, Angelini 1992, Rogers 1996, Papagno 2002, Trojano 2004).

Results of other studies provide support for right hemisphere involvement in constructional function. Poetzl (1928) conceded that the right hemisphere was involved in the maintenance of a temporo-spatial framework in which input from the environment may be interpreted. Later studies (Platz and Mauritz 1995, Smith and Gilchrist 2005) echo Poetzl's original suggestion concluding that patients with right hemisphere damage may have difficulty in making use of new sensorimotor information that is relevant for spatial motor activity. Piercy (1960) found that right temporo-parieto-occipito lesions appear most closely associated with the emergence of CA, which accords with CT findings in later studies of patients with CA (Ruessmann 1988). Other authors suggest that constructional impairment tends to be more common (Warrington 1990, Gheorgita 1980, Villa 1986) and more severe in patients with damage to the right parietal lobe (Hirschenfang 1960, de Ajuriaguerra 1960, Benton 1962, Arrigoni 1964, Black and Strub 1976, Hier et al 1983, Carlesimo et al 1993). Recovery from CA may also be relatively poor after right hemisphere damage (Sunderland 1994).

Overall, the results suggest that constructional difficulties may result from unilateral lesions of either hemisphere. This is consistent with neuroimaging studies of drawing movements in healthy adults showing that some individuals showing predominantly right activation and some left, regardless of handedness (Ino 2003, Makuuchi 2003). The possibility remains however, that each hemisphere may provide different contributions to the process of construction. For example, Warrington (1966) identified several differences between patients with left and right hemisphere lesions when copying geometrical figures. Left hemisphere patients were more likely to improve with practice than right hemisphere patients. She suggests that right hemisphere patients are liable to errors of proportion and spatial relationships due to impaired spatial articulation of drawings, and thus spatial co-ordinates cannot be used effectively to guide motor activity. Left hemisphere patients have difficulty planning the drawing and thus produce simplified versions that lack sufficient detail. These findings accord with other studies that support the notion of differential hemispheric contributions to constructional function (Paterson and Zangwill 1944, Duensing 1953, Piercy 1960, Arrigoni 1964, Hecaen and Assal 1970, McCarthy and Warrington 1990).

However, other reports do not support Warrington's findings. Arena and Gainotti (1978) and Gainotti (1985) found no differences in the nature of CA in patients with left and right hemisphere damage, with both groups having difficulty reproducing the spatial relations between different elements of the stimulus and a tendency to simplify the most difficult designs.

Trojano et al (1993, 2004) found no differences between patients left or right hemisphere damage when reproducing a complex figure, with both groups obtaining lower scores than controls. Simple analytical strategies predominated and were attributed to attentional deficits, which is believed to be an important factor in poor constructional skills in young children (Sutton and Rose 1998). Other studies have commented that performance of brain damaged adults on measures of constructional function tend to resemble those of young children when reproducing three-dimensional shapes (Griffiths et al 1988) or articulating oblique lines (Smith and Gilchrist 2005). Studies using callosotomy patients also attest to the notion of construction being subserved by both cerebral hemispheres, but suggest possible right hemisphere dominance. Several studies suggest that callosotomy patients perform more poorly on construction tasks when using the left hemisphere (Gazzaniga 1962, 1967, Bogen 1965), though performance with either hemisphere was lower than controls (Gazzaniga 1965, Geschwind 1979). The authors conclude that construction is a bilateral and integrated function. The left hemisphere may become more adept with practice (Gazzaniga 1967), though Le Doux (1978) attributes improved performance of the right hand to the increasing capacity of the right hemisphere to direct constructive functions of the right hand via ipsilateral control. It becomes clear that the debate surrounding possible contributions of the left and right cerebral hemispheres to constructional function is complex, and there are few recent replications of older studies to inform the debate. It is difficult to draw conclusions from available literature as studies differed according to tasks used and locus of cerebral lesions was not always specified. Further investigation is needed using a systematic battery of assessments with patients whose unilateral lesions are clearly specified.

7.1.2 The development of constructional skills

7.1.2.1 Stages of Normative Development

Piaget and Inhelder (1948; see also Luquet, 1913; 1927) described four basic developmental stages in children's drawings: (a) *Scribbling* (<2years) occurs prior to the emergence of preoperational thought. In this stage, children cannot accurately reproduce a model as drawings typically consist of lines and marks with no recognisable figures. (b) *Synthetic incapacity* (3-5 years) begins when children are entering preoperational thought and can draw an enclosed figure such as a square or a circle. In this stage children will attempt to add details, but spatial arrangement is often incorrect. Placement improves over this time, but perspective and proportion are still poor. (c) *Intellectual realism* (5-7 years) is the stage when proportion improves and placement of features becomes increasingly accurate. Basic shapes (circle, square, triangle) and lines (vertical, horizontal, oblique) are reproduced successfully at this stage and may be articulated to reproduce figures with multiple elements. The figure is often inaccurately drawn with respect to the perspective and proportion of the background and surrounding environment, as conceptual knowledge interferes with the production of visually accurate drawings. (d) *Visual realism* (8-9 years) occurs when children progress to concrete stages of thought and are able inhibit what is known about intrinsic object properties in order to draw a figure in proportion and in proper perspective with background features. Although the relationship between Piagetian stage of cognitive development and level of drawing ability may not in fact be linear (see Chappell & Steitz, 1993), authors agree that as cognitive development proceeds, so does drawing ability (Chappell & Steitz, 1993: Leeds, 1983).

Several authors (Chen and Cook 1984, Chen and Holman 1989, Costall 1995, Sutton and Rose 1998) suggest that intellectual and visual realism are not two distinct developmental stages in the development of drawing ability, instead reflecting two different strategies adopted by children when they are confronted with the problem of representing three dimensional objects. Sutton and Rose (1998) postulate that attentional engagement is a key factor in governing which strategy will dominate in the reproduction of a figure. As attentional functions become increasingly engaged in drawing, so does the tendency to adopt visual as opposed to intellectual realism in drawings. Sutton and Rose conclude that progression from intellectual to visual realism occurred between 6-8 years of age. Younger children are concerned primarily with drawing "a" model, whereas older children are concerned with drawing "the" model. Whilst younger children looked at the model only at the beginning of the task, older children continually checked their drawing with the model. Younger children could also be prompted into adopting visual realism by increasing the amount of attention paid to the model. Other authors have also found that increased attentional engagement resulted in more accurate drawings (Philips 1978, Wright-Rand 1973, Bremner et al 2000).

7.1.2.2 Children's Use of Graphic Formulas

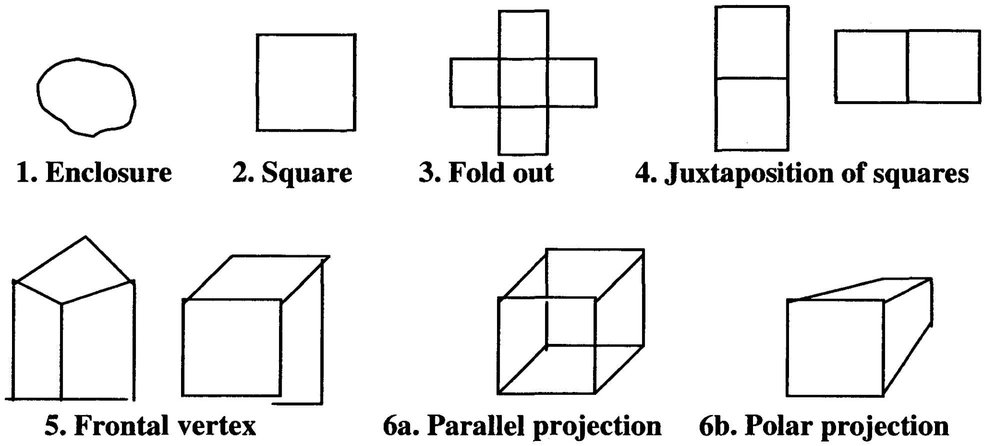
Drawing is a process whereby segments are recognised and their interrelations appreciated. These relations are then reconstructed in a particular spatiotemporal order to produce the figure. Both children and adults draw according to rules, and these 'graphic formulas' are evident by age 2 years (Wright-Rand, 1973, Fenson 1985, Freeman 1980, Stiles 1995, 1997). They simplify the problem of graphic representation by eliminating the requirement to analyse spatial properties of the model, and thus may be a particularly useful compensatory strategy in children with immature or impaired spatial analytic skills. Children often copy shapes in the same way and follow the same route when making repeated copies of a figure. Administration of rules for drawing enhanced children's attention to the model contour and resulted in better drawings (Wright-Rand 1973), which provides support for the role of attentional function and drawing accuracy as proposed by Sutton and Rose (1998). Karmiloff-Smith (1990) suggests that knowledge components embedded in previously established graphic formulas may then be subject to redescription to enable increasing cognitive sophistication and flexibility. Relaxation of constraints in graphic formulas enables introduction of subroutines and the establishment of inter-representational links to other conceptual categories. This is evident in drawings from 8-10 year olds, and may be involved in the acquisition of two milestones in drawing skills that appear relatively late in development: the ability to represent occluded objects, and the depiction of geometric shapes in three dimensions.

7.1.2.3 Drawing of Depth and 3-Dimensional Forms

Children often have difficulty accurately portraying depth via occlusion and 3-dimensional forms in their drawings. The elimination of hidden lines is a necessary prerequisite for the portrayal of depth between partially occluded objects (Willats 1977). If Children lack technical and organisational competence necessary for such eliminations, depth cannot be adequately represented, and the principal focus remains on the communication of object properties as opposed to spatial relationships. Ingram and Butterworth (1989) found that when children below 7 years of age are presented with an array of objects in depth they would portray them either vertically or horizontally in the picture plane (see also Cox 1980, Freeman 1977, Taguchi 2003). Radkey and Enns (1987) suggest that young children have difficulty selecting one perspective and maintaining it over another, which suggests failure to draw partially occluded objects is not merely a feature of immature motor skills, but also involves immature perspective taking. Willats (1997) described a transition in children's drawings from object centred topological space whereby objects are drawn without reference to viewpoint, through to viewer centred space, where the child reproduces objects that are relative to their line of sight. When applying this hypothesis to occluded figures, young children would draw separate figures to represent object properties at the expense of accurate depiction of viewpoint, whereas older children would violate what is conceptually known to draw what is actually seen, thus eliminating lines to depict occlusion. Bremner (1997) found that partial occlusions in drawings were evident by 9 years of age.

second key problem in graphic representation is the translation of three-dimensional reality into a two dimensional form on paper. An accurate copy of a cube involves replication of arrangement and orientation of lines, which in turn requires correct representation of angular relationships, a task that young children find particularly difficult (Bremner and Taylor 1982, Ibbotson and Bryant 1976). Moore (1987) and Bremner et al (1997) found that non-objects were drawn more accurately than familiar objects of similar complexity, supporting the proposal that drawings of familiar objects may be hindered by internal representations of a previously established prototype. When children are faced with a familiar object, the influence of internal representations of that object predisposes them to realist errors such as angle distortion and detracts from the accuracy of the reproduction. Intrinsic object properties are portrayed at the expense of viewpoint and thus the drawing is content as opposed to structure directed, as in occluded figures (Freeman 1972). Several authors propose distinct stages for cube drawing (Willats 1987, Caron-Pargue 1985), from simple enclosures in 3-4 year old children developing into single squares for 5 year olds, with subsequent juxtapositions of multiple squares that eventually undergo foreshortening to produce parallel projections in children aged 9 years and above.

Figure 7:1. Stages of cube drawing (from Willats 1987, Nicholls and Kennedy 1992)



Compromise between appearance and structure result in parallel projections as opposed to polar projections, and thus parallel projections represent a plateau where three-dimensional drawing skills tend to arrest in the majority of individuals (Golomb 1992). In a simpler formulation, Nicholls and Kennedy (1992) distinguish only two stages. One is an early stage peaking at around 5 years of age whereby a single square is drawn as a cube. The second is a later stage peaking at around 12-14 years of age in which the cube is drawn using parallel projection. There does not appear to be a distinct path between these two stages, with different individuals creating different types of intermediate. It is suggested that around 8 years of age, children are no longer concerned with geometrical similarity between object features and features on the page. This enables violations of conceptual knowledge and thus foreshortening occurs, with subsequent projection of depth. In summary, there is evidence that construction of more complex aspects of drawings such as depth and 3-dimensional information develops in stages over a protracted period in childhood, with mature drawings emerging between 10 - 14 years of age. It is of interest to determine whether brain injured children are able to reach this level of maturity in constructional function.

7.1.2.4 Effects of Lesions in Childhood

A few studies have examined drawing abilities in children with unilateral focal lesions. Although deficits appear to resolve with advancing age, the presentation of more challenging tasks may precipitate the re-emergence of characteristic impairments observed earlier in life. Stiles (1997) questions the apparent functional recovery of constructional function children with early unilateral brain injury and suggests that compensatory strategies may be employed to bypass persistent impairments in visuospatial cognition. A house drawing task (Stiles 1997) revealed that, like adults, young children with left hemisphere lesions have difficulties processing pattern detail, whereas children with right hemisphere damage have difficulties organising components of an array into accurate spatial configurations. The latter result echoes findings in an earlier study (Stiles 1988). Although drawings improve with increasing age due to the use of graphic formulas, there is considerable reluctance in manipulating spatial aspects of drawings, which suggests that the formulas are relatively rigid and constrained due to persistent impairment in spatial function.

Akshoomoff (2002) used the Rey Complex Figure Test (RCFT) to measure visuospatial construction, planning and memory skills in children with unilateral cerebral lesions. The RCFT is particularly challenging until age 9, at which point children can adequately produce a copy (Waber and Holmes 1985, Akshoomoff and Stiles 1995). Drawings from children with early left hemisphere injury demonstrated inaccurate use of details, whereas drawings from children with right hemisphere injury lacked configural elements, although both patient groups omitted and misplaced more elements of the figure than neurologically intact controls. By 10 years of age, both patient groups were able to reproduce reasonably accurate copies, though immature piecemeal strategies were used. These results suggest that different patterns of impairment seen in children may be related to side of injury, although these differences may become less pronounced with age as children's abilities improve and they develop a strategy of relying on graphic formulas to produce reasonably accurate drawings. This may help to explain why several studies documenting constructional function in adults failed to find side specific differences (Trojano 2004).

Most of the studies documenting visual cognition in hemispherectomised patients included some measures of constructional ability. Case studies generally report impaired constructional function. Left hemispherectomised patient MP demonstrated generally poor performance on copying a 3D drawing of a house (Marriotti 1998). Ogden (1989) also reported impoverished design copy in left hemispherectomised patients KOF and JSY, and Chiricozzi (2005) reports similar findings for right hemispherectomised case GT. Comparison of left and right hemispherectomised patients does not generally reveal side specific differences, though two studies exist that comment on such differences. Strauss and verity (1983) found that free drawings of left hemispherectomised patients lacked detail, whereas drawings from right hemispherectomy patients were spatially inaccurate. Spencer-Day and Ulatowska (1979) also comment on impoverished detail in free drawings and copies of left hemispherectomy patient SD, whereas right hemispherectomised case DP demonstrated generally immature reproductions, with no distinct profile specified. Gott (1973) reported impaired free drawings and design copy scores in both left and right hemispherectomised patients but reproduction of details versus configuration was not reported. In a larger study of 71 hemispherectomised cases, Pulsifer (2004) also found that design copy was impaired regardless of side of hemispheric injury, though no details are given beyond scaled scores. Use of generally small sample sizes and inconsistencies across studies in terms of tasks used may account for these heterogenous findings. There are no studies to date that have exclusively addressed the issue of constructional function in hemispherectomised patients, resulting in a lack of detailed assessments of milestones such as depiction of occlusion and 3D figures. In the light of this, and Kohn and Dennis' (1974) proposal that spatial maturity of the left hemisphere may not progress beyond that of a child aged 10:0, it is of interest to determine the integrity of constructional function in hemispherectomised patients.

7.2 Aims and predictions

The principal aims of this neuropsychological study of constructional function in hemispherectomised patients were (1) to characterize the nature and extent of any impairment in this domain; (2) to determine the relationship between side of hemispheric injury and task performance; (3) to determine whether constructional function is more efficient when mediated by two functional cerebral hemispheres (4) to examine the influence of age at seizure onset and duration of seizure disorder on task performance.

Within and between groups comparisons of neuropsychological data from the patient and control groups were carried out. The predictions were as follows:

- Intellectual realism would predominate in three-dimensional drawings as a function of immature construction skills.
- Left hemispherectomy patients would be more likely to show omission of details in constructions than right hemispherectomy patients and controls.
- Right hemispherectomy patients would be more likely to show spatial disorganisation in constructions than left hemispherectomy patients and controls.
- Right hemispherectomy patients will therefore obtain lower scores on three dimensional drawings.

- Constructional ability will be positively correlated with age at seizure onset in the left hemispherectomy group as visuospatial functions in the right hemisphere become increasingly impervious to the effects of crowding.

7.3 Methods

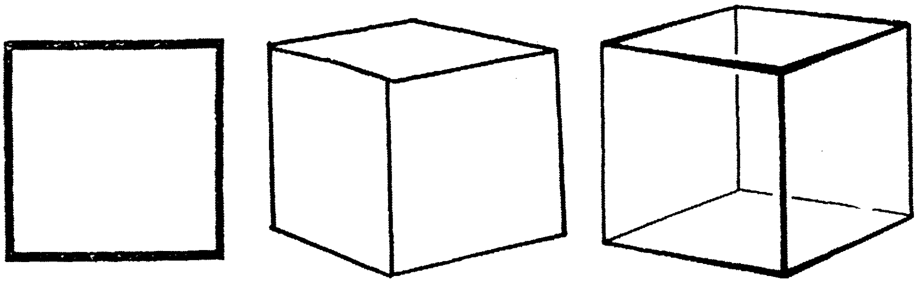
7.3.1 The Test of Visuomotor Integration

The Test of Visuomotor Integration (Beery 1989) was administered to provide a measure of the ability to copy both simple and relatively complex shapes as a function of visual perception and fine motor co-ordination. The test consists of a booklet containing 24 line drawings of shapes and geometric figures, each with a space below it in which the subject is required to draw a copy of the shape. Shapes are presented in increasing order of difficulty, and the subject has 5 minutes to complete the test. Visual perception and motor co-ordination abilities related to the test are assessed using supplemental assessments that involve shape discrimination and drawing using line guides respectively. For the test proper, each of the 24 shapes are awarded a number of score points on a pass/fail basis, with a maximum total score of 50 points for the test. The total score is then converted into a scaled score and an age equivalent using the test manual. Scores from motor co ordination (MC) and visual perception (VP) tests were also converted to scaled scores and age equivalents using the test manual. Cube drawing skills were measured in the VMI and shapes challenge tests using a 6 stage system based on those constructed by Willats (1985) and Caron-Pargue (1985). Mastery of each stage was awarded one point hence a stage 6 cube was awarded a score of six points. Examples of each stage were shown in Figure 7.1.

7.3.2 The Shapes Challenge Test

The Shapes Challenge test was designed to provide a measure of the ability to copy progressively complex geometrical shapes. It provides additional information to the VMI, which contains only one example of a 3 dimensional stimulus, which can be reproduced using a previously learned graphic formula that bypasses most of the spatial processing load of reproducing 3 dimensional stimuli. Several authors have noted the importance of 3D drawings in uncovering otherwise silent constructional difficulties (Critchley 1953,Warrington et al 1966, Griffiths et al 1988). The test consists of a booklet containing 24 line drawings of shapes (six 2D, eighteen 3D shapes), each with a space below it in which the subject is required to draw a copy of the shape. The test includes both opaque and transparent figures. Shapes are presented in increasing order of difficulty according to number of parts to be articulated, and there is no time limit in which to complete the test. Each shape is awarded one point if drawn correctly for a total of 24 possible points. Correct drawings included all of the following criteria: correct number of parts, appropriately oriented edges and lines, and correct articulation of parts.

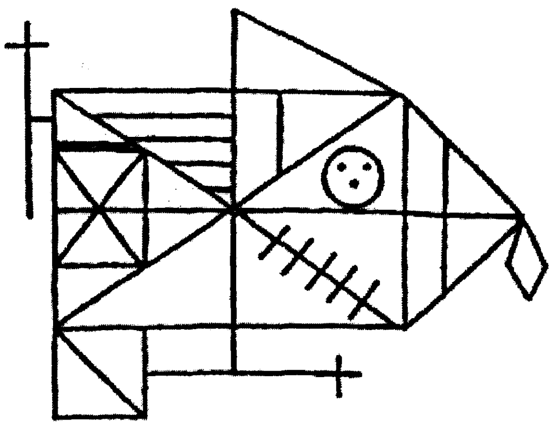
Figure 7:2. Shapes challenge test – square, opaque cube and transparent cube.



7.3.3 The Rey Complex Figure Test

The Rey Complex Figure Test (Rey 1941, Osterrieth 1944) was administered to provide a measure of constructional function as a function of visual organisation, motor planning and graphomotor ability, in addition to recall and recognition capacity of visual memory. The test consists of a reproduction of the complex figure, which the subject is required to copy, using a pencil and an A4 sheet of paper. Subjects are not allowed to rotate either the design or the paper so that rotational errors and difficulties working with the unrotated figure are apparent. Once the figure has been copied, the design and the subject's copy are removed from view. The subject is asked to draw the figure from memory 3 minutes later. After completing the second reproduction there is a 30 minute delay, after which the subject is required to make another reproduction from memory.

Figure 7:3. The Rey complex figure



The original copy and the two reproductions are scored according to the number of elements correctly drawn and placed, with each drawing scoring a maximum of 36 points. The final part of the assessment is a recognition test. The subject is presented with a selection of small designs, half of which were elements of the original figure. The subject is required to select the designs that were pieces of the original figure whilst rejecting distractor items. Subjects score one point for each item correctly recognised or rejected, with a maximum of 24 points. False positive and false negative recognition items are also recorded.

The Boston Qualitative Scoring system (BQSS, Stern et al 1994) was used to investigate inclusion and placement of different elements of the figure (details, clusters and configurations). Percentage of elements correctly included and placed are scored on a 1-5 scale, where a score of 1 = 0-24%, 2 = 25-33%, 3 = 34-67%, 4 = 68-89%, 5 = 90-100%.

7.4 Analyses

Analyses of neuropsychological data were carried out as described in chapter 2. Covariates used in ANCOVA were age at test and PIQ. ANOVA design and factors will be referred to throughout the results section as appropriate.

7.5 Results

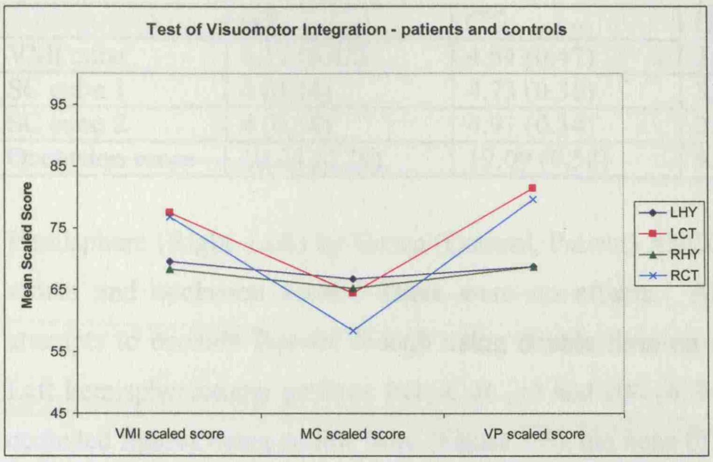
7.5.1 The Test of Visuomotor Integration

Table 7.1, and figure 7.4 summarises the results for the patient and control groups for the test of visuomotor integration. Repeated measures ANCOVA was used to examine differences between scores of the different components of the VMI test. The within subjects factor *sub test* comprised of 3 levels pertaining to scaled scores for the test proper, the motor co-ordination and visual perception supplements. Between subjects factors of group (Control, patient) and hemisphere (Right, left) were also included. Evidence for an interaction between sub test and group was observed (ANCOVA: $F\ (2,34) = 7.67$, $p = .002$), suggesting differences in score profiles between patients and controls. Independent samples t tests were used to examine differences between patients and controls on the three components of the test of visuomotor integration. Bonferroni correction was applied to adjust for multiple comparisons. VP scaled scores ($t = 3.0$, $p = .005$) were higher in the control group.

Table 7.1. Test of Visuomotor Integration scores (mean +/- SEM)

	HY_L (N= 12)	CT_L (N= 11)	HY_R (N= 10)	CT_R (N= 8)
VMI scaled score	69.5 (3.81)	77.45 (3.41)	68.3 (3.02)	76.71 (5.33)
Age equivalent of mean	8:4	10:4	8:1	9:10
MC scaled score	66.75 (3.36)	64.45 (2.49)	65.2 (3.54)	58.29 (5.63)
Age equivalent of mean	7.5	7	7:3	6:6
VP scaled score	68.67 (4.68)	81.45 (3.59)	68.7 (2.97)	79.57 (4.65)
Age equivalent of mean	8:1	10:5	7:7	9:8

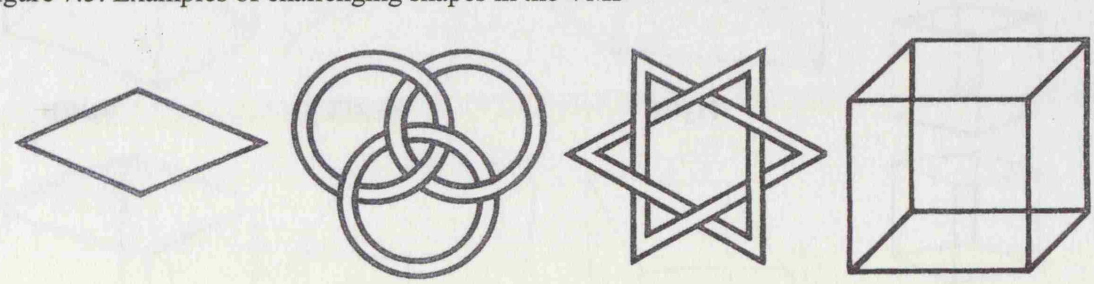
Figure 7:4. VMI total scores for patients and controls



A closer look at individual scores on the VMI test reveals that none of the hemispherectomy patients obtained age appropriate scores, though some participants obtained scores above that of a child aged 10 years of age. Left hemispherectomy cases **HW** $_L$**6**, **TS** $_L$**11** and **JL** $_L$**12** and right hemispherectomy cases **KD** $_R$**8** and **EBK** $_R$**10** obtained age equivalent scores between 11:2 – 13:8. Controls demonstrated a similar pattern, with just 2 subjects obtaining age appropriate scores, and 5 controls obtaining age equivalent scores between 10:4 – 13:5.

It is of note that shapes that caused difficulty could be grouped into 4 categories: diamonds, shapes with a superimposed element, occluded shapes and the 3D cube (see Figure 7.5). Normative data from the test manual suggest that diamonds tend to be mastered by 11 years of age, three-dimensional cubes by 12 years of age, and superimpositions and occluded figures are mastered by 13 years of age. As the majority of participants obtained an age equivalent below that at which these milestones are achieved, it seems that drawing skills had not reached sufficient levels of maturity to accurately reproduce shapes within these categories.

Figure 7:5. Examples of challenging shapes in the VMI



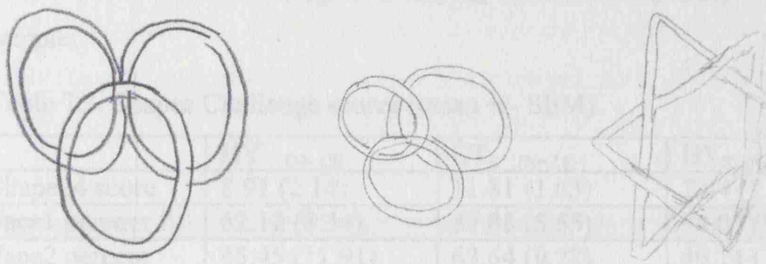
In the light of the results, a measure of the ability to draw occluded figures was calculated based on performance on shapes 13, 19, 21 and 24, yielding a total score of 14 (3 points each for shapes 13 and 19, 4 points each for shapes 21 and 24 as stated in the test manual).

Table 7.2. Cube scores and occlusion scores (mean +/- SEM).

	HY_L (N= 12)	CT_L (N= 11)	HY_R (N= 10)	CT_R (N= 8)
VMI cube	4.17 (0.42)	4.64 (0.47)	3.9 (0.5)	4.71 (0.71)
SC cube 1	4 (0.44)	4.73 (0.36)	3.9 (0.54)	5 (0.53)
SC cube 2	4 (0.38)	4.91 (0.34)	3.9 (0.51)	4.71 (0.61)
Occlusion score	10.04 (0.79)	12.09 (0.58)	9.35 (0.89)	11.43 (0.9)

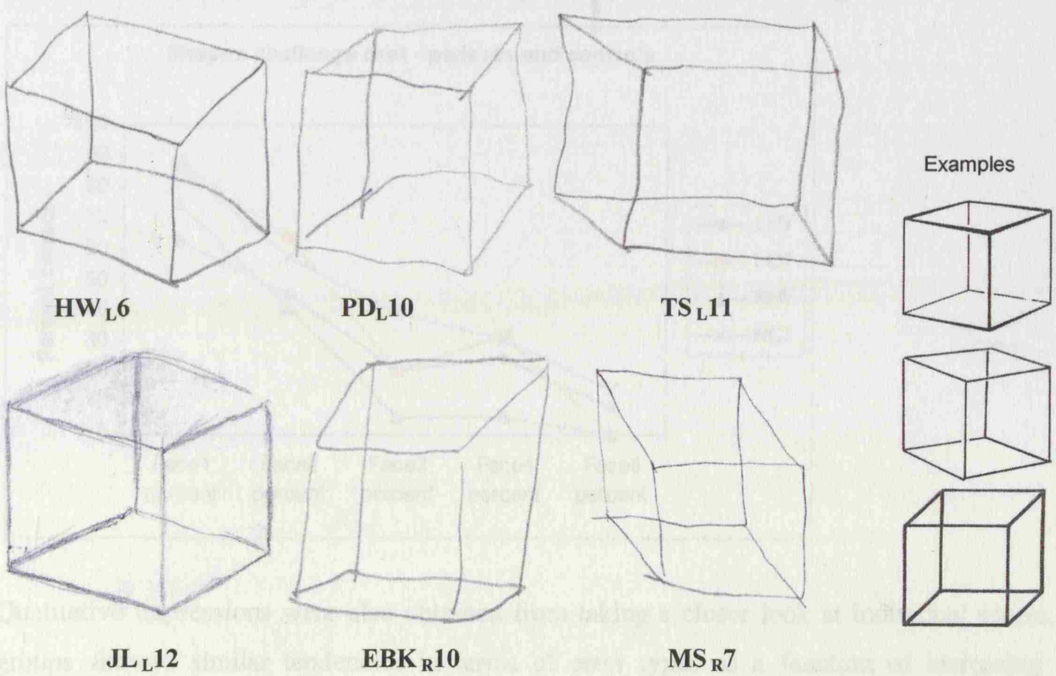
Hemisphere (Right, Left) by Group (Control, Patient) ANCOVA was computed for mean cube scores and occlusion scores. There were no effects. All participants demonstrated some attempts to occlude figures, though using double lines on shapes 21 and 24 proved difficult. Left hemispherectomy patients **RG $_L$4**, **JL $_L$12** and **HW $_L$6** demonstrated some attempts to draw occluded figures using double lines (Figure 7.6), but none of the right hemispherectomy patients were able to do so. 6 control subjects (3 left, 3 right) also demonstrated appropriate occlusion on shapes 21 and 24.

Figure 7:6. Occluded Figure drawings – Left hemispherectomy patients



RG $_L$4 shape 21 **HW $_L$6 shape 21** **JL $_L$12 shape 24**

Figure 7:7. Cube drawings – hemispherectomy patients



All participants had mastered at least stage 2 of cube drawing, with the majority of participants obtaining level 3 or more. Left hemispherectomy patients **HW$_L$6, PD$_L$10, TS$_L$11** and **JL$_L$12** and right hemispherectomy cases **GB$_R$4** , **EBK$_R$10** and **MS$_R$7** demonstrated use of parallel projection to successfully depict 3 dimensional cubes (Figure 7.7). 4 left controls and 3 right controls also demonstrated this strategy..

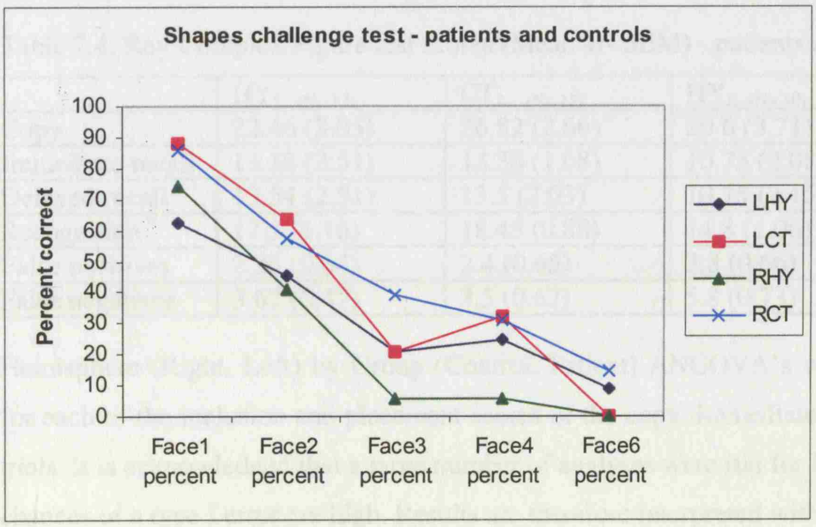
7.5.2 The Shapes Challenge (SC) Test

Table 7.3 and figure 7.8 summarise the results for the patient and control groups. Repeated measures ANCOVA was used to examine differences between scores for shapes of different levels of complexity. The within subjects factor "faces" was comprised of 5 levels, corresponding to scores for shapes with 1, 2, 3, 4 or 6 faces. Between subjects factors of hemisphere (left vs right) and group (patient vs control) were included. Evidence for a main effect of "faces" was observed (ANCOVA: $F(2,35) = 3.76$, $p = .011$), confirming that differences in scores for shapes of varying levels of complexity were apparent within the study sample.

Table 7.3. Shapes Challenge scores (mean +/- SEM).

	HY_L (N= 12)	CT_L (N= 11)	HY_R (N= 10)	CT_R (N= 8)
Shape24 score	8.91 (2.14)	11.81 (1.63)	7.44 (1.3)	12.29 (2.82)
Face1 percent	62.12 (8.34)	87.88 (5.55)	74.07 (8.83)	85.71 (9.22)
Face2 percent	45.45 (11.91)	63.64 (9.22)	40.74 (11.49)	57.14 (14.48)
Face3 percent	20.45 (9.43)	20.45 (9.43)	5.55 (3.67)	39.29 (18.79)
Face4 percent	24.24 (8.1)	31.82 (10.16)	5.55 (2.78)	30.95 (14.29)
Face6 percent	9.1 (9.1)	0	0	14.29 (14.29)

Figure 7:8. Shapes challenge scores according to number of faces on a figure.



Qualitative impressions were also obtained from taking a closer look at individual scores. All groups showed similar tendencies in terms of error types as a function of increasing task difficulty. It appeared that simple shapes were susceptible to rounded edges and misorientation of lines between two parts. More complex shapes were more susceptible to omission of parts and failure to articulate parts, resulting in grossly simplified drawings. Left hemispherectomy cases **HW $_L$6, PD$_L$10, TS $_L$11** and **JL $_L$12** successfully attempted some of the transparent shapes requiring articulation of 3 or more faces, whilst none of the right hemispherectomy cases demonstrated accurate production of transparent drawings requiring articulation of more than two parts. 5 left and 3 right control subjects also demonstrated correct articulation of transparent shapes with 3 or more faces.

7.5.3 The Rey Complex Figure test

Table 7.4 summarises the results obtained for the Rey Complex Figure test. Hemisphere (Right, Left) by Group (Control, Patient) ANCOVA's were computed separately for recognition, false positives and false negatives. Evidence for an interaction between group and side was observed for number of false negatives on the recognition trial (ANCOVA: $F (1,33) = 4.81$, $p =. 036$). Exploration of this interaction using t tests revealed that right hemispherectomy patients produced more false negatives than left hemispherectomy patients ($t = -2.55$, $p = .019$). There were no other interactions for any of the variables listed above. It was therefore appropriate to look at main effects. Evidence for a main effect of group was found for total score obtained on the recognition trial (ANCOVA: $F (1,35) = 5.97$, $p = .02$), with patients performing more poorly than controls. Repeated measures ANCOVA was used to examine differences between scores obtained in copy, immediate recall and delayed recall trials for the study groups. The factor "Rey" had 3 levels; copy score, immediate recall score and delayed recall score. Between subjects factors of hemisphere (left vs right) and group (patient vs control) were also included. There was no evidence for any interactions or main effects.

Table 7.4. Rey Complex Figure test scores (Mean +/- SEM) - patients and controls.

	HY_L (N= 12)	CT_L (N= 11)	HY_R (N= 10)	CT_R (N= 8)
Copy	22.46 (3.05)	26.82 (2.66)	20.6 (3.71)	27.86 (3.37)
Immediate recall	13.38 (2.51)	13.36 (1.68)	10.75 (2.08)	14.57 (3.09)
Delayed recall	13.54 (2.51)	13.5 (2.03)	10.75 (2.15)	15.14 (2.85)
Recognition	17.5 (1.16)	18.45 (0.88)	14.8 (1.06)	18.85 (0.86)
False positives	2.25 (0.64)	2.4 (0.65)	2.8 (0.66)	1.85 (0.86)
False negatives	3.67 (0.47)	3.5 (0.62)	5.8 (0.73)	3.14 (0.63)

Hemisphere (Right, Left) by Group (Control, Patient) ANCOVA's were computed separately for each of the inclusion and placement scores of the copy, immediate recall and delayed recall trials. It is acknowledged that a large number of analyses were run for BQSS scores and thus the chances of a type I error are high. Results are therefore interpreted with caution. Evidence for an interaction between group and side was observed for cluster inclusion on the delayed recall trial (ANCOVA F 1,35 = 5.27, $p =. 028$). Exploration of this interaction using t tests revealed that right hemispherectomy patients omitted more clusters on the delayed recall trial than left hemispherectomy patients (t = -2.25, p = .035) but this did not survive Bonferroni correction. There were no other interactions for any of the variables listed above. It was therefore appropriate to look at main effects. Evidence for a main effect of group was found for cluster placement in the delayed recall trial (ANCOVA F 1,35 = 4.41, p =. 043), with patients performing more poorly than controls. The main effect of group for cluster placement in the immediate recall trial (ANCOVA F 1,35 = 3.98, p = 0.054) was just outside statistical significance.

Correlational analyses were run to determine the relationships between copy and recall scores. Scores for the copy trial of the RCFT positively correlated with immediate recall (left hemispherectomy group: R = .837, p = .001, left control group: R = .68, p = .021, right hemispherectomy group: R = .725, p = .018) and delayed recall (left hemispherectomy group: R = .825, p = .001, right hemispherectomy group: R = .788, p = .007). Accurate copies are thus associated with better recall of the figure.

Figure 7:9. BQSS scores for the copy trial – patients and controls.

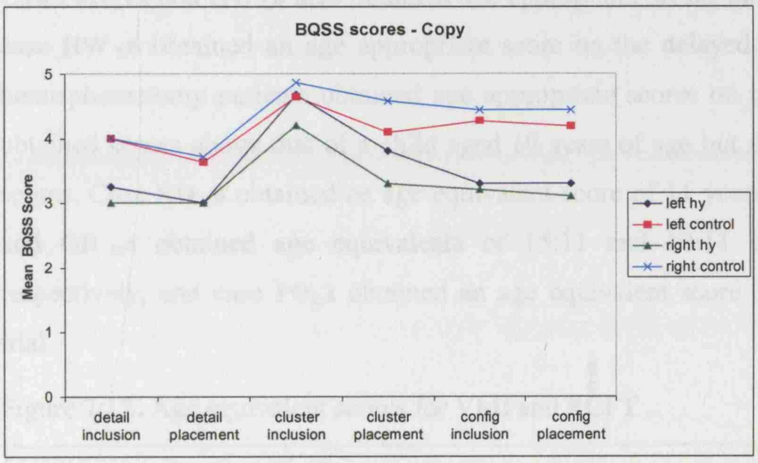


Figure 7:10. BQSS scores for the immediate recall trial – patients and controls.

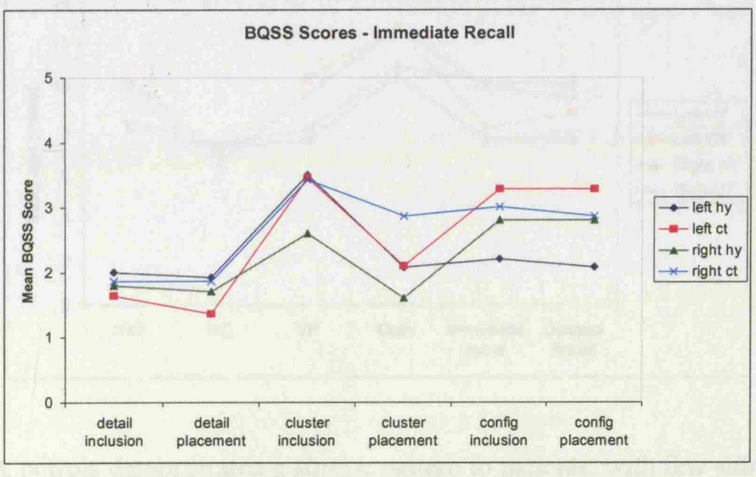
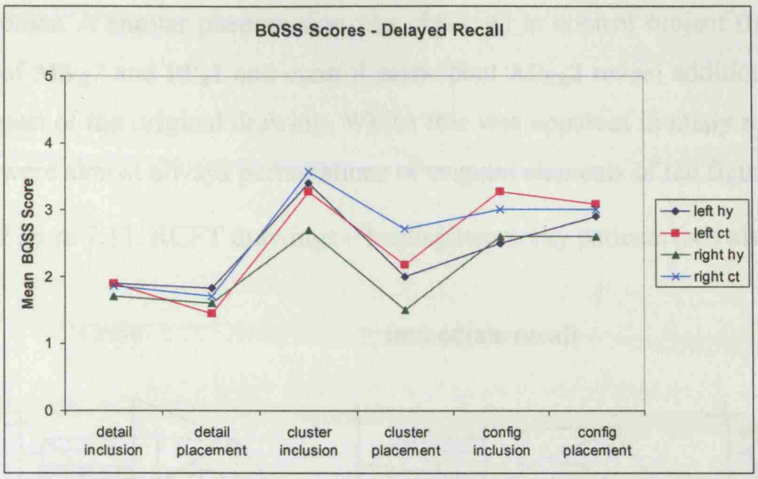
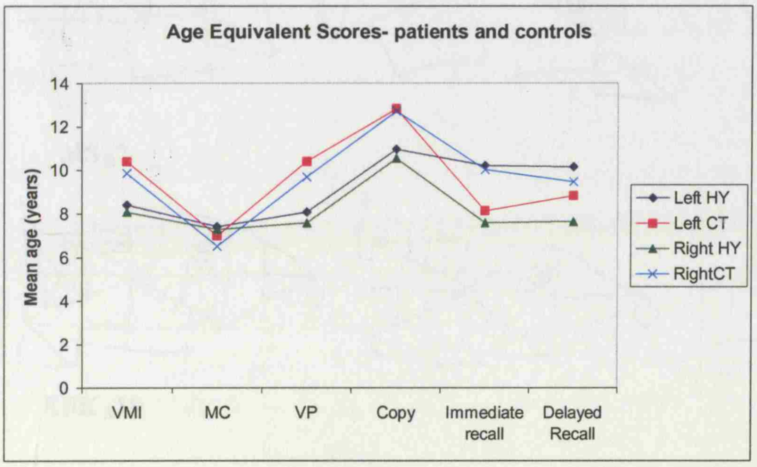


Figure 7:11. BQSS scores for the delayed recall trial – patients and controls.



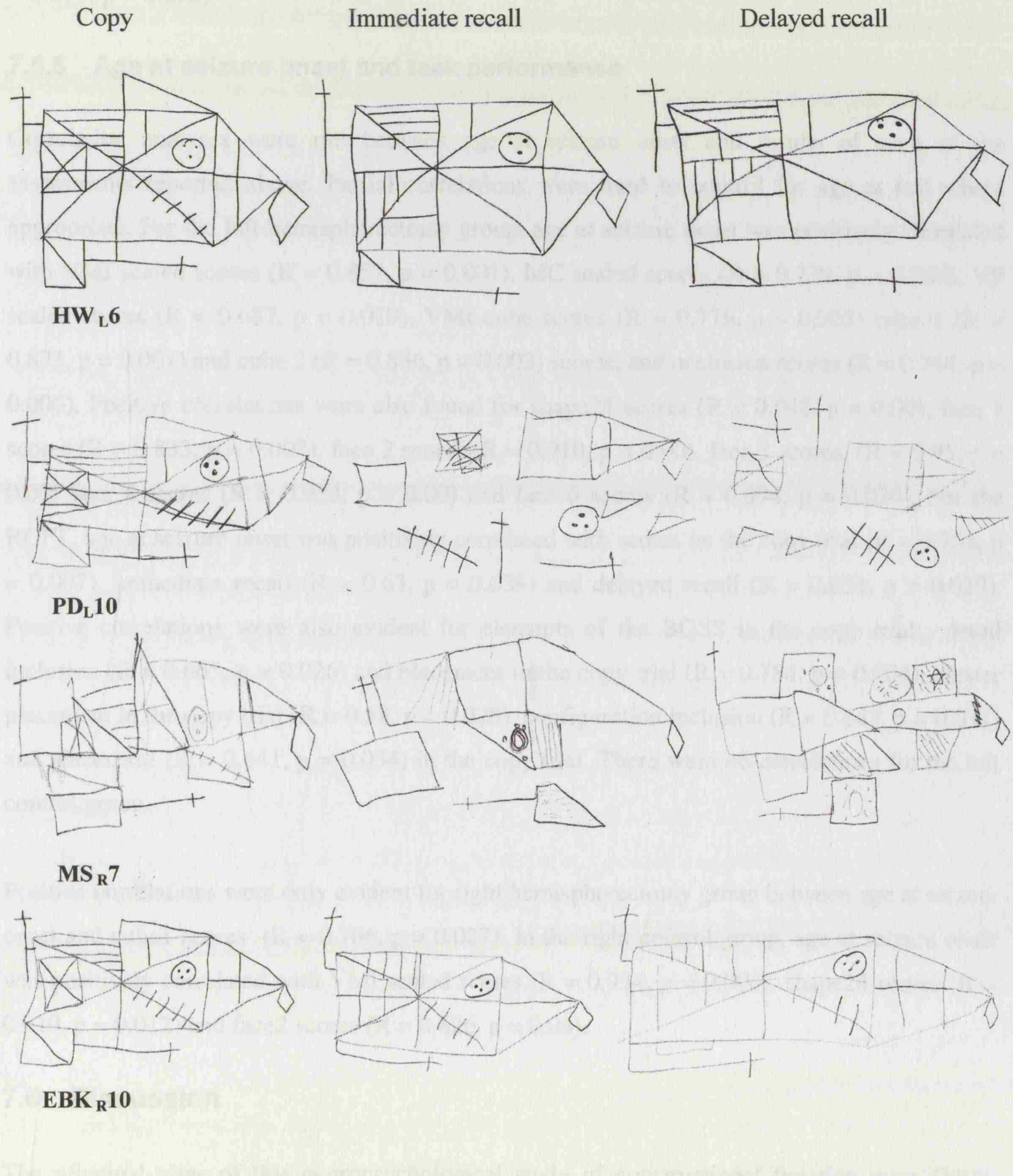
A closer look at individual cases reveals that several patients obtained age appropriate scores on the RCFT. Left hemispherectomy cases **HW $_L$6, PD$_L$10, TS $_L$11** and **JL $_L$12** and right hemispherectomy cases **GB $_R$4** and **EBK $_R$10** obtained age appropriate scores on the copy trial. Cases **JL $_L$12** and **HW $_L$6** also obtained age appropriate scores on the immediate recall trial, and case **HW $_L$6** obtained an age appropriate score on the delayed recall trial. None of the right hemispherectomy patients obtained age appropriate scores on the recall trials. Some patients obtained scores above that of a child aged 10 years of age but failed to obtain age appropriate scores. Case **KD $_R$8** obtained an age equivalent score of 11 years on the copy trial, cases **PO$_L$2** and **GB $_R$4** obtained age equivalents of 15:11 and 10:11 on the immediate recall trial respectively, and case **PO$_L$2** obtained an age equivalent score of 15:11 on the delayed recall trial.

Figure 7:12. Age equivalent scores for VMI and RCFT



Controls demonstrated a similar pattern to patients, with few subjects obtaining age appropriate scores, but 10 controls obtained age equivalent scores above 10 years of age on the copy trial, 4 subjects on the immediate recall trial and 6 subjects on the delayed recall trial. It was of note that case **PD$_L$10** could only recall isolated details that could not be placed in relation to each other. A similar phenomenon was observed in control subject **DD$_{CR}$6**. Delayed recall drawings of **MS$_R$7** and **PP$_R$1** and control participant **AD$_{CR}$2** reveal addition of extra details that were not part of the original drawing. Whilst this was apparent in many reproductions, additional details were almost always permutations of original elements of the figure.

Figure 7:13. RCFT drawings – hemispherectomy patients (see also fig 7.3)



7.5.4 Construction and general intelligence

Partial correlations controlling for age at test were used to determine whether PIQ scores and performance on construction tasks were associated. VMI scaled scores, Cube scores, occlusion scores, shapes challenge total scores, and RCFT copy, immediate and delayed recall scores were examined. For the left hemispherectomy group, PIQ scores correlated with VMI total scores ($R = 0.803$, $p = 0.001$), VMI visual perception scores ($R = 0.803$, $p = 0.001$), cube ($R = 0.70$, $p = 0.016$), occlusion ($R = 0.643$, $p = 0.033$) and shapes challenge scores ($R = 0.88$, $p = 0.001$). There were no correlations for the left control group. PIQ scores in right hemispherectomy patients correlated with VMI ($R = 0.837$, $p = 0.005$) and occlusion ($R = 0.734$, $p = 0.005$) scores. PIQ scores in right control participants correlated with VMI visual perception scores ($R = 0.877$, $p = 0.022$).

7.5.5 Age at seizure onset and task performance

Correlation analyses were run between age at seizure onset and results of each of the assessments reported above. Partial correlations were used to control for age at test where appropriate. For the left hemispherectomy group, age at seizure onset was positively correlated with VMI scaled scores ($R = 0.857$, $p = 0.001$), MC scaled scores ($R = 0.739$, $p = 0.009$), VP scaled scores ($R = 0.687$, $p = 0.019$), VMI cube scores ($R = 0.776$, $p = 0.005$) cube 1 ($R = 0.873$, $p = 0.001$) and cube 2 ($R = 0.836$, $p = 0.003$) scores, and occlusion scores ($R = 0.764$, $p = 0.006$). Positive correlations were also found for shape24 scores ($R = 0.948$, $p = 0.00$), face 1 scores ($R = 0.833$, $p = 0.003$), face 2 scores ($R = 0.910$, $p = 0.00$), face 3 scores, ($R = 0.95$, $p = 0.00$) face 4 scores ($R = 0.923$, $p = 0.00$) and face 6 scores ($R = 0.694$, $p = 0.026$). For the RCFT, age at seizure onset was positively correlated with scores on the copy trial ($R = 0.755$, $p = 0.007$), immediate recall ($R = 0.63$, $p = 0.038$) and delayed recall ($R = 0.654$, $p = 0.029$). Positive correlations were also evident for elements of the BQSS in the copy trial: detail inclusion ($R = 0.665$, $p = 0.026$) and placement in the copy trial ($R = 0.784$, $p = 0.004$), cluster placement in the copy trial ($R = 0.58$, $p = 0.028$), configuration inclusion ($R = 0.647$, $p = 0.031$) and placement ($R = 0.641$, $p = 0.034$) in the copy trial. There were no correlations for the left control group.

Positive correlations were only evident for right hemispherectomy group between age at seizure onset and cube1 scores ($R = 0.766$, $p = 0.027$). In the right control group, age at seizure onset was positively correlated with VMI scaled scores ($R = 0.934$, $p = 0.006$), shape24 scores ($R = 0.910$, $p = 0.012$) and face2 scores ($R = 0.826$, $p = 0.04$).

7.6 Discussion

The principal aims of this neuropsychological study of constructional function were (1) to characterize the nature and extent of any impairment in this domain in patients and controls; (2) to determine the relationship between side of hemispheric injury and task performance; (3) to determine whether constructional function is more efficient when mediated by two functional cerebral hemispheres (4) to address the issue of age at seizure onset on task performance.

7.6.1 The integrity of drawing ability after hemispherectomy

7.6.1.1 Test of Visuomotor integration (VMI) and shapes challenge

Overall, the results from the VMI suggest that rudimentary constructional skills as measured by copy drawings appear to be intact in the isolated left and right hemispheres, and approximate those found in a child aged 8 years of age. Although it is acknowledged that 9 patients obtained scores above the mean, there were no age appropriate scores. Mean scores in the control group approximated those of a child aged 10 years of age, with 7 controls scoring above the mean, including 2 age appropriate scores. These results illustrate limitations in construction skills across the study sample, resulting in immature reproduction attempts that may or may not result in success, depending on the complexity of the stimulus. These findings accord with previous studies (Griffiths et al 1988, Stiles et al 1997, Smith and Gilchrist 2005) that suggest patients with brain injuries tend towards immature drawing skills whatever the locus of cerebral injury. Circles, squares and triangles were reproduced successfully, as were vertical, horizontal and oblique single lines. Performance tended to decline as shapes included diamonds, shapes with a superimposed element, occluded shapes and three-dimensional figures, which are beyond the repertoire of drawing skills possessed by the majority of study participants. These shapes require acute attention to detail to ensure correct reproduction of angles (Broderick and Laszlo 1987, Bremner et al 2000), part-whole relationships and portrayal of depth in the picture plane, as prior knowledge may initiate content directed drawings that reflect what is inherently known about shapes as opposed to what is actually seen (Freeman 1980). When considering the stages of drawing development outlined in section 7.1.2.1, it appears that the majority of study participants have reached a level of drawing ability pertaining to synthetic incapacity or intellectual realism, depending on the complexity of the model to be copied. As the transition from intellectual to visual realism may occur around 9 years of age (Piaget and Inhelder 1948, Nicholls and Kennedy 1992, Bremner et al 1997), it may be the case that constructional function in hemispherectomised patients and controls is just below the developmental level at which visual realism begins to dominate drawings, which accords with age equivalent scores in this study being situated between 8-10 years of age. An alternative suggestion proposed by Sutton and Rose was that inadequate attention might prevent demonstration of visual realism. This could account for the fact that some individuals (**$\mathbf{TS_L11}$, $\mathbf{KD_R8}$** and **$\mathbf{EBK_R10}$**) that obtained scores equivalent to or above the age at which visual realism emerges still demonstrate a tendency towards intellectual realism. Conversely, it may also explain why case **$\mathbf{RG_L4}$** is able to reproduce features such as occlusion using double lines, and cube drawings that include some foreshortening of receding edges whilst obtaining an age equivalent score of 6:7.

The majority of study participants had difficulties reproducing more advanced items of the VMI. Previous studies have documented the fact that children have difficulty drawing diamonds yet squares are reproduced successfully (Naeli and Harris 1976, Broderick and Laszlo 1987). Such difficulties are believed to stem from greater planning and programming demands when drawing and articulating oblique lines (Bremner and Taylor 1982). Indeed, errors were either distortions of angulation (overly acute or obtuse) or line size. Age norms for successful reproduction of diamonds range between 8:1 – 10:11 (VMI manual), which may explain why these shapes proved difficult for study participants. Occlusion scores and cube drawings enabled further investigation of the presence of intellectual as opposed to visual realism in drawings. All participants demonstrated some attempts to occlude figures as opposed to drawing them separately, suggesting development of occlusion skills beyond those observed in children below 7 years of age (Ingram and Butter worth 1989, Bremner 1997) though using double lines on shapes 21 and 24 proved difficult. Left hemispherectomy patients **RG$_{L}$4**, **JL$_{L}$12** and **HW$_{L}$6** demonstrated attempts to draw occluded figures using hidden double lines, and 6 control subjects (3 left, 3 right) also demonstrated the same approach on shapes 21 and 24. These results suggest that attempts to produce visually realistic drawings in the form of occluded figures is apparent in all cases when simple single line figures are to be reproduced, but performance declines when double line figures are used, with only a handful of participants able to successfully depict occlusion. Even when appropriate attempts to occlude were evident, figures were often only partially correct (see figure 7.6). The key difficulties in successful reproduction were correct orientation of figures and elimination of hidden lines, which accords with previous studies of drawing occluded figures (Willats 1977, Ingram and Butterworth 1989) and the scoring system in the VMI manual.

All participants had mastered at least Willats stage 2 of cube drawing, though the majority of participants reproduced cubes below Willats stage 6, which suggests that object knowledge was predominant in reproductions as opposed to perceived stimulus properties from a particular viewpoint. Left hemispherectomy patients **HW$_{L}$6** and **PD$_{L}$10** and right hemispherectomised patient **GB$_{R}$4** demonstrated use of parallel projection to successfully depict one of the 3 dimensional cubes within the VMI or shapes challenge test, though it is of note that they were only successful on one of the three cubes, implying use of a graphic formula that failed when cube orientation changed. Cube drawings either lapsed from stage 6 to stage 5, or a stage 6 cube was drawn that was a mirror image of the model, reflecting difficulties reproducing the new orientation. Similar findings were noted in control participants **LW$_{CL}$10** and **AD$_{CR}$2**. Cases **TS**

$_{L}$**11, JL**$_{L}$**12, MS**$_{R}$**7** and **EBK**$_{R}$**10** were successful on at least two of the cubes, which suggests that in some cases, the isolated hemisphere is able to inhibit or violate conceptual knowledge and use viewpoint specific visual information to produce visually realistic drawings. A similar pattern was evident in reproductions of other 3D items in the shapes challenge test. Complex shapes were more susceptible to simplification, misorientation and depiction of discrete object components as opposed to production of coherently articulated figures, though some left hemispherectomy patients (**HW** $_{L}$**6, PD**$_{L}$**10, TS** $_{L}$**11, JL** $_{L}$**12**) were able to reproduce accurate drawings of shapes with multiple faces.

Collectively, results from direct reproduction tests suggest that the majority of patients and controls reach a developmental plateau that renders drawings susceptible to intellectual realism and inflexible graphic formulas that may persist into adult life (as evidenced by participants aged 18:0 and above). This tendency appears to increase when shapes have occluded elements, multiple faces and are drawn in three dimensions. The finding of impaired performance in some hemispherectomised patients and intact performance in others accords with previous studies documenting constructional function after hemispherectomy (Smith 1969, Gott 1973, Spencer-Day 1979, Strauss and Verity 1983, Sergent and Villemure 1989, Ogden 1989, Marriotti 1998, Pulsifer 2004, Chiricozzi et al 2005). Conflicting findings in some of these studies may result from using very small patient samples, thus failing to represent the spectrum of possible outcomes. Pulsifer's report encompasses a large cohort of hemispherectomised patients, and the finding of generally impaired performance on the VMI accords with results in this thesis. There is no further analysis of strengths and weaknesses of performance on the VMI however, and it is therefore unclear whether specific limitations observed in patients reported in this thesis match those of Pulsifers cohort. The interaction between attention and visual realism in hemispherectomy patients would be an interesting avenue of enquiry in future work, and may represent a strategy whereby constructional skills could be enhanced by encouraging increased attentional engagement to the target stimulus.

7.6.1.2 The Rey Complex Figure Test

The Rey Complex Figure Test provided an additional level of complexity via copy, recall and recognition trials of a multi-element abstract 2D stimulus. Results were similar to the VMI in terms of a general lack of age appropriate performance and accord with Ogden's (1989) study documenting impaired performance on the RCFT. Mean scores for copy and recall trials across study groups had age equivalents between 10:6 – 12:10 and 7:6 – 10:1 respectively. Most patients were able to accurately recall and recognise at least some elements of the figure, indicating that the isolated hemisphere has a rudimentary capacity to reproduce abstract drawings from memory, though in some cases this ability is extremely limited, and sometimes paradoxical to current consensus, as in the case of **PD$_{L}$10**, whose piecemeal reproduction of the figure with an isolated right hemisphere is at odds with reports of simplified but configurally adequate reproductions in patients with left hemisphere disease (Akshoomoff 2002). The relationship between good constructional skills and success on the copy trial of this task was illustrated by cases **HW$_{L}$6, PD$_{L}$10, TS$_{L}$11** and **JL$_{L}$12** and right hemispherectomy cases **GB$_{R}$4** and **EBK$_{R}$10**, all of whom produced age appropriate copies of the figure and obtained above average scores on the shapes challenge test. Cases **JL$_{L}$12** and **HW$_{L}$6** also obtained age appropriate scores on the immediate recall trial, and case **HW$_{L}$6** obtained an age appropriate score on the delayed recall trial, which implies that manual reproduction of visual stimuli may operate successfully from images in addition to percepts in the isolated right hemisphere.

7.6.1.3 General Cognitive Impairments and Construction

It is important to keep in mind when interpreting the results of both the patient and control groups that constructional skills may be impaired as a result of general cognitive impairments (Warrington 1966, Villa 1986, Maeshima 2002). Stiers (2001) suggests that a global visual perceptual deficiency can exist in children with pre and perinatal brain damage, and thus poor drawing skills, may be attributed to immature information processing and working memory limitations as positive correlations between IQ measures and drawing task measures were found. It is therefore possible that progression from intellectual to visual realism is paralleled by increases in general non-verbal cognitive ability, which accords with the consensus that as cognitive development proceeds so does drawing ability (Chappell & Steitz, 1993: Leeds, 1983). These observations may have implications for interpretation of performance on constructional assessments, as although spatial cognitive deficits may result in constructional deficits, constructional skills may also be disrupted as a result of general cognitive impairments related to immature information processing. Indeed, Stiers found that children with learning difficulties encountered problems with spatial integration leading to simplified, stereotyped drawings.

An intermediate position is most likely, as results from the current study do not support a straightforward relationship between PIQ scores and performance on construction tasks. The fact that most study participants demonstrate impaired performance on both PIQ subtests and construction measures is supportive of the prediction in section 7.2 regarding predominance of intellectual realism in drawings as a function of generic reduction in cognitive function, but significant correlations between PIQ and construction test scores were only abundant for the left hemispherectomy group. There are also three hemispherectomy patients with Performance IQ within the average range (**HW$_{L}$6, JL$_{L}$12, EBK$_{R}$10**), whose scores on constructional tests are below age appropriate levels. Their PIQ matched controls often failed to achieve age appropriate scores only when the task involved a memory component (RCFT immediate and delayed recall). The dissociation between PIQ and construction skills accords with findings from Akshoomoff's study when using the RCFT in brain damaged children with average PIQ's. It is therefore possible that constructional deficits can be dissociated from reduced non-verbal intelligence in some cases, particularly when non verbal intelligence scores approach the average range. This in turn suggests that constructional function may be selectively impaired when childhood cerebral injury occurs, which provides some support for prioritisation of linguistic functions and "crowding out" of visual cognitive function (Teuber 1975).

7.6.2 Comparison of left and right hemispherectomised patients

7.6.2.1 Test of visuomotor integration and shapes challenge test

There did not appear to be any group differences between left and right hemispherectomy patients on drawing measures which did not confirm the predictions in section 7.2 regarding side specific differences, and a number of cases in both groups demonstrated mastery of certain elements of constructional function in these assessments. These results question the notion of each hemisphere providing different contributions to the process of construction (Paterson and Zangwill 1944, McFie et al 1950, Spencer-Day and Ulatowska 1979, Strauss and Verity 1983, McCarthy and Warrington 1990, Stiles 1996, 1997, Akshoomoff 2002). Although some variables such as effects of practice were not assessed in this study, errors of simplification and elaboration of irrelevant detail, overly acute and obtuse angles, and errors of proportion and spatial relationships were examined, and performance was found to be broadly similar in left and right hemispherectomy patients. These observations accord with previous suggestions that damage to either hemisphere may result in disturbance of constructional function and produce similar patterns of impairment (Arena 1978, Gainotti 1985, Binder 1982, Trojano 1993, 2004). The overall lack of differences between left and right hemispherectomised patient groups may also be attributed to task demands being placed on both segmentation and integration in the majority of items in tests used in this study, as many stimuli had multiple elements (Benson and Barton 1970, Wright-Rand 1973). Such items would require segmental analysis of a structured whole in terms of identification of component parts, and holistic appreciation of part-whole relationships.

A closer look at individual scores however, did reveal some differences between patient groups. It is acknowledged that these observations were not qualified by statistical analysis due to small numbers and are therefore interpreted cautiously. The shapes challenge test proved difficult for the majority of study participants, although left hemispherectomy cases **HW$_L$6, PD$_L$10, TS$_L$11** and **JL$_L$12** successfully attempted some of the transparent shapes requiring articulation of 3 or more faces. 5 left and 3 right control subjects also demonstrated correct articulation of transparent shapes at this level, yet none of the right hemispherectomy cases demonstrated accurate production of transparent drawings requiring articulation of more than two parts. These findings imply that spatial integrative functions may indeed tend towards immaturity in the isolated left hemisphere, as proposed by several authors (Gainotti and Tiacci 1970, Kohn 1974, Stiles 1988, 1997). Although some transparent figures were successfully articulated in the right hemispherectomy group, they were misoriented and were thus possibly the product of a graphic formula as opposed to a drawing of what was actually presented. Similar observations were recorded for occluded figures, as none of the right hemispherectomy patients were able to demonstrate occlusion using double lines. Difficulties may represent intellectual realism and inability to modify existing graphic formulas to reproduce viewpoint specific examples of a shape, which agrees with Stiles (1997) proposal that children with right hemisphere injury bypass spatial processing difficulties by execution of graphic formulas. In this case, the execution of a formula is at the expense of accurate reproduction, and may represent failure to effect re-representation of internal descriptions to allow cognitive flexibility upon encounter of a novel stimulus (Karmiloff-Smith 1990).

7.6.2.2 The Rey Complex Figure Test

Previous studies (Piercy et al 1960, Warrington 1966, Gainotti and Tiacci 1970) suggested that adult patients with right hemisphere damage are prone to adding extraneous detail to drawings. This phenomenon was observed in the RCFT recall trials in three cases; right hemispherectomy cases **PP**$_{\mathbf{R}}$**1** and **MS** $_{\mathbf{R}}$**7**, and right control subject **AD**$_{\mathbf{CR}}$**2**. Several authors also suggest that patients with left hemisphere lesions produce simplified versions that lack sufficient detail (Warrington et al 1966, Gainotti and Tiacci 1970, Akshoomoff 2002). There was no evidence to suggest that left hemispherectomy patients produced drawings that were more simplified than right hemispherectomy patients, with scores for copy trials of all tasks being similar across the two patient groups, hence the prediction in section 7.2 was not confirmed. When considering Kohn and Dennis' (1974) proposal that visuospatial skills in the isolated left hemisphere are unlikely to mature beyond 10 years of age, it is of note that **GB** $_{\mathbf{R}}$**4**, **KD** $_{\mathbf{R}}$**8** and **EBK** $_{\mathbf{R}}$**10** produced copies of the Rey complex figure that were beyond this level of maturity, and **KD** $_{\mathbf{R}}$**8** and **EBK** $_{\mathbf{R}}$**10** obtained scores on the VMI equivalent to 11 years 2 months. These findings highlight the importance of acknowledging task specific effects and small sample sizes when drawing general conclusions about the limits of function in the isolated hemispheres.

Comparison of RCFT data with Akshoomoff's (2002) study of children with unilateral cerebral injury revealed some discrepancies between results obtained in that study and the current analysis, though it is acknowledged that younger children with higher IQ and a slightly different paradigm (no delayed recall or recognition trials) were used in the Akshoomoff study. Scores for "details" and "configurations" in the copy trial were similar for left and right hemispherectomy patients in this thesis, whereas side specific effects were found in the Akshoomoff study. No differences in immediate recall performance were found in either study. In the current analysis, right hemispherectomy patients were less likely to recall clusters of the Rey Complex Figure after a delay of 30 minutes and in turn produced more false negatives in the recognition trial. As the majority of the items in the recognition trial incorporate cluster material, it seems that failure to retrieve cluster information may be responsible for both group differences observed in the RCFT. This remains speculative however as results that suggested differences in cluster inclusion scores did not survive correction for multiple comparisons and may therefore represent a type I error in statistical analysis. Detailed assessment of visual memory was beyond the scope of this thesis and represents an interesting avenue of further enquiry.

Another interesting observation in the recall trials of the RCFT involved left hemispherectomy patient **PD_L10**. Although his copy of the figure was age appropriate, both immediate and delayed recall consisted of a collection of elements of the figure with no accompanying knowledge as to their location within the figure. A similar phenomenon was noted in right control subject **$DD_{CR}6$**. These examples of piecemeal reproduction in the absence of spatial context appear to contradict proposals that drawings of left hemisphere patients are simplified and lack detail (Warrington 1966), though it is acknowledged that this assertion is based on only one case. Nevertheless, other studies have argued that an intact right hemisphere does not guarantee holistic visuospatial processing (Binder 1982, Trojano 1993) and results from **PD_L10** lend weight to this proposal.

Thus, it seems that subtle differences may exist between left and right hemispherectomy patients, but they are apparent only when tasks include complex stimuli or the inclusion of a memory component, a rationale that has been utilised in other studies of laterality of visual cognitive function such as global and local processing (Delis et al 1986, 1988, Dukette and Stiles 1996). Overall, these findings do not provide strong support for theories of early hemispheric specialisation and studies documenting side specific effects of early cerebral lesions on constructional function, though further study is required using tasks that address issues of stimulus complexity and memory demands. The small number of cases that obtained good scores suggests that attention to and reproduction of detail and spatial organisation in drawings may develop and function efficiently in either lone hemisphere, suggesting some degree of equipotentiality for constructional function.

7.6.3 One versus two functional hemispheres

Overall, there were very few differences between scores obtained by hemispherectomised patients and controls. This suggests that in the context of general cognitive impairment, constructional function reaches similar levels of maturity in the lone hemisphere and in the bihemispheric brain. It is acknowledged however that visual perception scores on the VMI were higher in the control group. This implies that the execution phase of construction as assessed by the motor co-ordination subtest may be superior to the perception and translation phase as assessed by the visual perception test in the isolated hemisphere. The presence of hemianopia was an unlikely factor contributing to this result, as stimuli were presented vertically in each trial of the visual perception subtest. All study participants were able to reproduce simple items, and very few participants were able to reproduce more complex items. It therefore seems likely that task complexity may be an important factor in eliciting differences between patients and controls such that certain stimuli may be of sufficient but not excessive complexity to unveil differences between individuals with one versus two functional hemispheres. A similar rationale was proposed in the previous section when examining differences between the isolated left and right hemispheres. Differences between patients and controls were also apparent in the recall and recognition trials of the RCFT, with cluster placement in recall trials and total recognition scores being higher in controls. Group differences in recall and recognition ability may be related to differences in visual perceptual skills as demonstrated on the Test of Visuomotor integration, as efficient stimulus analysis and registration may in turn affect subsequent recognition and recall of target components. The exact nature of group differences regarding stimulus perception, reproduction and recognition remains to be elucidated, but it is possible that attentional factors influence performance. Several authors suggest that constructional function improves with increasing attentional capacity (Wright-Rand 1973, Sutton and Rose 1998, Bremner et al 2000). Differences between patients and controls in attentional functions described in chapter 4 may contribute directly or indirectly to group differences in the current chapter as a function of reduced attentional engagement during the reproduction process. It would be of interest to determine whether patient – control differences were attenuated by encouraging increased attentional engagement during constructional tasks.

7.6.4 Effects of Age at Seizure Onset and related variables

Positive correlations between age at seizure onset and scores on the VMI, SC and RCFT assessments in the left hemispherectomy group were encouraging with respect to the possibility of an interaction between developmental stage and reorganisation of function. Visual perception, motor co-ordination and visuomotor integration measures were all positively correlated with age at seizure onset. More detailed measures such as cube drawing and occlusion scores were also correlated, in addition to copy and recall performance on the RCFT. These results are interpreted with caution due to small sample sizes, but it remains possible that as development proceeds, the repertoire of constructional function within the right hemisphere may become increasingly impervious to the effects of reorganisation of function in the event of left hemisphere damage, which accords with the crowding hypothesis. Some positive correlations were also observed in the right control group, though most tasks did not correlate with age at seizure onset, and so the relationship between age at seizure onset and the development of constructional skills in the bihemispheric brain in this study is less clear. It remains possible that there is a more general advantage of later onset of seizures for perseveration of constructional function, though it is difficult to reconcile this possibility with the lack of correlations observed in left control subjects and right hemispherectomy patients. These possibilities remain to be elucidated with larger sample sizes and other paediatric epilepsy cohorts.

7.6.5 Summary

In summary, the results suggest that rudimentary constructional skills as measured by copy drawings appear to be intact in the isolated left and right hemispheres. Difficulties articulating more complex drawings reflect immature reproduction attempts that may be subject to intellectual realism. Exceptions did exist however, which suggests that in some cases, the isolated hemisphere is able to inhibit or violate conceptual knowledge and use viewpoint specific visual information to produce visually realistic drawings. Hemisphere specific differences were only apparent when tasks involved complex stimuli or a memory component, which seemed to favour the isolated right hemisphere. Patient – control differences were also subject to task complexity effects, and findings suggest that the execution phase of construction may be superior to the perception and translation phase in the isolated hemisphere. Correlations between task performance and age at seizure onset imply that as development proceeds, the repertoire of constructional function within the right hemisphere may become increasingly impervious to the effects of reorganisation of function in the event of left hemisphere damage, which accords with the crowding hypothesis.

8 General discussion

The investigations reported in this thesis were designed to examine visual cognitive abilities following hemispherectomy for intractable childhood epilepsy. Comparisons were made to a group of control participants with epilepsy that had not undergone this surgical procedure. There were four primary aims that were addressed in each chapter. The first aim was to characterise the nature and extent of any impairment in visual cognition in these patients in an attempt to contribute to what is currently a small amount of available literature. The second aim was to establish whether any differences were apparent between patients according to side of hemispheric removal, to add to the debate surrounding laterality of function in the developing brain in terms of competing theories of early specialisation, equipotentiality and interactive specialisation. The third aim was to determine whether visual cognitive impairments in hemispherectomised patients were related to generic reduction of cognitive function or cognising with a lone hemisphere. This is an important point that is often neglected in hemispherectomy outcome studies. The fourth aim was to determine the relationship between age at seizure onset and visual cognitive ability in an attempt to assess the crowding hypothesis.

The results of neuropsychological and experimental investigations will be summarised for each chapter according to each of the above four aims (see appendix F for brief summary table of significant results for each chapter) and discussed in relation to previous research. Limitations of the current study will be addressed where appropriate, and suggestions for future research are also included.

8.1 Visual cognitive function after hemispherectomy

The comprehensive evaluation of visual cognitive function in hemispherectomised patients provides convergent evidence to suggest that a broad spectrum of possible outcomes is evident. The majority of individuals demonstrate impaired performance relative to the neurologically intact population, as evidenced by a general lack of age appropriate scores across hemispherectomised patient and control groups. Results are consistent with previous hemispherectomy outcome studies using smaller groups (see section 1.5.9) that document generally intact (Damasio 1975, Smith and Sugar 1975, Sergent and Villemure 1989, Vanlancker 2004) and impaired (Smith 1969, Gott 1973, Kohn and Dennis 1974, Spencer and Ulatowska 1979, Strauss and Verity 1983, Ogden 1989, Marriotti 1998, Pulsifer et al 2004, Chiricozzi 2005) visual cognitive abilities after hemispherectomy. The advantage of using a larger group was that the data in this thesis supported seemingly opposing views in smaller studies, with each stance in these smaller studies representing a fraction of possible outcomes. A larger study group would have been preferable, as it would have been interesting to group patients according to type of pathology. Previous studies using larger samples (n = 40-70) have suggested that patients with dysplastic lesions have less favourable outcomes after hemispherectomy due to persistent seizure activity (Doring 1999, Curtiss and de Bode 2001, Pulsifer 2004). Only one of these studies to date has included a measure of visual cognitive function – the test of visuomotor integration (Pulsifer et al 2004), and the finding of impaired performance on this test regardless of side of hemispheric removal accords with results in this thesis. Time constraints and the rarity of the patient group precluded using sample sizes similar to the studies mentioned above, but it remains a viable possibility for future research to explore the relationship between aetiology of cerebral insult and visual cognitive outcome.

Impaired general intellectual function in hemispherectomised patients is a well established finding (see chapter 2), and is attributed to the deleterious effects of brain injury and seizures as opposed to hemispheric removal per se as there is often no further detriment to cognitive function after surgery (Vining 1997, Devlin 2003, Pulsifer 2004). Pre- and post-operative data were not compared in this study, as the vast majority of tests in this thesis were not used in pre-operative assessments of these patients. Incorporation of a systematic and comprehensive battery of neuropsychological tests designed to assess visual cognitive function would be a valuable addition to pre-operative assessments to chart the trajectory of development of these functions during the course of the seizure disorder and to observe any changes apparent after surgery.

Findings in this study suggest that verbal and non verbal intelligence are similarly impaired in the hemispherectomised group which accords with previous group studies (Kohn and Dennis 1974, Dennis and Whitaker 1976, Verity 1982, Vargha-Khadem 1991, Kalkanis 1996, Pulsifer 2004), though others suggest a discrepancy in favour of verbal intelligence (St-James Roberts 1981, Strauss and Verity 1983, Battaglia 1999). A recurrent problem in studies using groups that vary widely in cognitive performance as in this thesis, is that potentially interesting observations become diluted by averaging performance across groups. A closer look at individual cases suggested that verbal-performance IQ discrepancies were usually in favour of the former, providing some support for the idea of verbal functions being prioritised relative to visual cognitive functions (Teuber 1975, Ogden 1989, Marriotti 1998) though it is acknowledged this was not supported by statistically significant findings from group comparisons. When considering the source of such a discrepancy, there were no obvious common factors shared by individuals with a VIQ-PIQ discrepancy favouring VIQ (congenital vs acquired injury, age at seizure onset, duration of seizure disorder, age at surgery, side of hemispheric removal, post surgical recovery period – see chapter 2, tables 2.2 and 2.3). There were however significant positive correlations between age at seizure onset and performance IQ measures for both left and right hemispherectomised patients, lending further weight to the concept of crowding, which is discussed in section 8.4. It is also possible that VIQ-PIQ discrepancies simply reflect difficulties completing motor loaded tasks of the PIQ scale within the time limits set (Muter et al 1997), a possibility that is particularly salient for the hemispherectomised patients due to hemiplegia, though it remains to be seen why a subset of controls also demonstrate a similar discrepancy in the absence of hemiplegia.

Due to limitations of the Wechsler scales in providing a comprehensive assessment of visual cognition, a detailed battery of neuropsychological tests were administered and reported in chapters 3 to 7. Impaired performance, particularly on more complex tasks was found in all groups regardless of side of hemispheric removal and the presence of one versus two hemispheres, and was consistent with generic reduction of cognitive function. Results echo those from measures of general intellectual function in that a broad spectrum of abilities was observed. Performance was generally intact for visual search with simple conjunctions and low distractor target ratios (chapter 4), indicating that the lone hemisphere possesses a working model of visual attention as defined by Treisman (1998), and Posner and Peterson (1990). Results from tasks involving face stimuli (chapter 5) also confirm the presence of a working model of face processing as defined by Bruce and Young (1986). Estimating age and gender of facial stimuli, categorisation of facial expressions into positive and negative emotions, recognising familiar faces and discriminating faces according to featural cues were evident in the majority of hemispherectomised patients and their controls. Spatial processing tasks (chapter 6) revealed that most patients were able to compute spatial relationships using egocentric co-ordinates to maintain a sense of left and right, mentally rotate 2D stimuli between 30-120 degrees and offer explanations of their strategy after metacognitive introspection, and compute spatial relationships using basic categorical and metric co-ordinates. Manual reproduction of simple shapes in drawing tasks was also apparent (chapter 7). These findings suggest that the isolated left or right hemisphere can develop and/or sustain a range of visual cognitive functions albeit in a limited manner, which is consistent with the presence of generalised cognitive impairment. Most of the abilities outlined above are within the grasp of a neurologically intact child aged between 6-9 years. In accordance with these assertions, difficulties were noted on tasks usually completed efficiently by neurologically intact children aged beyond 9 years, namely complex visual search (high distractor-target ratio – chapter 4), sub-categorising negative facial emotional expressions, discriminating faces according to configural cues (chapter 5), computing spatial relations using allocentric co-ordinates, mental rotation of stimuli with large angular rotations, computing spatial relationships using metric co-ordinates in a multifaceted array (chapter 6), and drawing shapes with oblique, hidden or foreshortened lines (chapter 7). There were also very few hemispherectomised patients and controls obtaining age appropriate scores on copy and recall trials of the Rey complex figure test (chapter 7). Collectively these observations suggest that visual cognitive abilities remain immature in the majority of individuals, which accords with previous suggestions from hemispherectomy outcome studies (Spencer and Ulatowska 1979, Strauss and Verity 1983, Pulsifer et al 2004). This thesis has also expanded on what has been previously reported on visual cognitive outcome in hemispherectomised patients by using a detailed battery of assessments across several domains of function. Previous reports have been limited in scope either by restricted coverage of different aspects of visual cognitive function, and/or reporting data from single cases or very small groups (n = 1-8). Use of a limited range of assessments in hemispherectomy outcome studies often provides an incomplete view of the actual limit of cognitive function in a particular domain because tests used may be too easy or too difficult. Use of small sample sizes can generate a narrow impression of visual cognitive abilities in hemispherectomised patients, leading to conflicting findings across studies. It becomes clear when using a detailed range of assessments in a relatively large hemispherectomised patient sample that a wide spectrum of performance exists, though the majority of participants demonstrate impaired visual cognitive abilities. Whether this represents failure to develop mature cognitive skills or regression of previously attained milestones in patients with later onset of epilepsy remains to be elucidated with longitudinal studies that address pre- and post-operative levels of function. As mentioned earlier, available literature suggests that there is little overall change between pre- and post-operative levels of cognitive function (Ignelzi and Bucy 1968, Vining 1997, Pulsifer 2004), including studies that incorporate some of the hemispherectomised patients from this study (Devlin et al 2003). It must be acknowledged however that pre-operative cognitive assessments may take place many months or years after onset of seizures, and so the question of regression versus failure to develop certain skills may remain unanswered. In addition, these studies tend to report results from IQ tests, hence comparison of pre- and post-operative levels of function in hemispherectomised patients on tasks specifically designed to assess visual cognitive functions remains elusive.

It is of note that patients with performance IQ within the average range (**HW $_L$6**, **JL $_L$12**, **EBK $_R$10**) demonstrated impaired performance on more detailed measures of visual cognition suggesting the relationship between general non verbal intelligence and visual cognitive abilities is not entirely linear. Regarding visual search tasks (chapter 4), **HW $_L$6** obtained a total score below the cut off on the Balloons B test, and all 3 cases failed to obtain age appropriate scores on the sky search and map mission tests. Difficulties were also apparent on the Ekman faces test (chapter 5), where stimuli had an inter-rater reliability of at least 90 percent, yet scores for these patients were between 67-75 percent. **EBK $_R$10** also failed to achieve age appropriate scores on the configural set of the Jane task. Regarding tests of spatial processing (chapter 6), **JL $_L$12** scored below the cut off for the Benton left-right orientation test, **HW $_L$6** scored below the cut off for the money road map test, and **EBK $_R$10** scored close to chance for the axis tests. Tests of constructional function (chapter 7) also reveal deficits in performance, as none of the three cases obtained age appropriate scores on the VMI. Scores for matched control participants of these 3 cases were similarly impaired for sky search, map mission and Ekman faces tasks, supporting the dissociation between levels of general intellectual function and visual cognitive ability when PIQ scores are within the average range. This accords with findings in previous studies using very small groups of hemispherectomised patients that illustrate dissociations between general intelligence levels and visual cognitive function (Ogden 1988, 1989, Mariotti 1998), again illustrating the merits of using larger groups and a detailed battery of assessments to gain a better overall impression of the range of outcomes after hemispherectomy. It is also of note that there are no examples of test results in this thesis where these PIQ intact cases provide the only examples of age appropriate or above cut off level scores. This suggests that intact PIQ is not always a necessary prerequisite for obtaining age appropriate scores in tests of visual cognitive function. Factors contributing to adequate performance remain to be elucidated, as cases demonstrating age appropriate performance varied widely in terms of aetiology of cerebral pathology, age at seizure onset, duration of seizure disorder, age at surgery and post surgical recovery period.

8.2 Comparison of left and right hemispherectomised patients

The anatomy of the visual system (detailed in chapter 1) suggests that either hemisphere has the basic neural architecture necessary for subserving visual cognitive function. There is available evidence however to suggest that functional specialisation of the cerebral hemispheres is evident in neurologically intact (De Schonen and Mathivet 1990, Koening et al 1990, de Haan and Nelson 1997) and brain injured children (Stiles 1997, Chiang et al 2000, Akshoomoff 2002, Meletti 2003, Schatz et al 2004). These observations lend weight to theories of early hemispheric specialisation, but it is of note that evidence is mixed regarding laterality of visual cognitive function in children, and there is often a paucity of data from which to draw conclusions. Indeed, most of the literature supporting hemispheric lateralisation of function comes from studies of neurologically intact (Ashbridge 1997, Nobre et al 2001, Noesselt et al 2005) and brain injured adults with focal unilateral lesions (Priftis et al 2003, Joubert et al 2003, Feigenbaum and Morris 2004, Schiltz et al 2005, Smith and Gilchrist 2005). It is acknowledged that one task in this thesis did illustrate statistically significant differences between left and right hemispherectomy patients, though results did not survive correction for multiple comparisons and are therefore interpreted with caution. Right hemispherectomised patients recognised and recalled fewer elements of the Rey complex figure, which accords with previous work suggesting right hemisphere lesions disrupt visual memory (Loring et al 1988, Piguet et al 1994, Breier et al 1996 but see Barr et al 1997), although this relationship is not always clear when lesions are sustained in childhood (Lippe and Lassonde 2004). The domain of visual memory was not investigated further in this thesis due to time constraints, and it is not possible at present to determine whether group differences were due to generalised or visual-specific memory impairment. Further study is required, with a detailed battery of assessments focused on different aspects of visual memory. This would also enable assessment of Gott's (1973) assumption that memory is selectively vulnerable in hemispherectomy patients and that it is essentially a bihemispheric function.

In contrast to theories of early specialisation, competing theories suggest that the two hemispheres are equipotent early in life (Lenneberg 1967, Vargha-Khadem 1992, Johnson 2000), with relative specialisations becoming apparent in later childhood. It was therefore of interest to compare performance in left and right hemispherectomy patients in this study for several reasons. Demonstration of classic hemispheric differences in left and right hemispherectomised patients would have provided support for theories of early specialisation, in that the lone hemisphere cannot compensate for skills usually subserved by the absent counterpart. Conversely, lack of differences between these patients would support the notion that the two hemispheres are equipotent, and will develop and/or maintain skills that are vital for independent survival. Indeed, the results of this thesis support the latter assertion in that almost no differences were found during group comparisons of left and right hemispherectomised patients. Lack of side specific deficits in this study accord with other hemispherectomy outcome studies suggesting general depression of cognitive function without side specific differences (Griffiths 1966, Ignelzi and Bucy 1968, Gott 1973, Dennis and Whittaker 1976, Spencer and Ulatowska 1979, Strauss and Verity 1983, Vargha-Khadem 1991, Kalkanis 1996, Pulsifer et al 2004) yet other studies argue for lateralised profiles (Kohn and Dennis 1974, Ogden 1988, Sergent and Villemure 1989). It is of note that studies advocating laterality of visual cognitive function after hemispherectomy often have small cohorts of usually less than six patients, and/or IQ measures that approach the average range. This may represent selection bias, thus failing to give a true general impression of abilities of left and right hemispherectomised patients. The presence of subtle bilateral damage also cannot be ruled out, which may contribute to observed impairments in visual cognition in these patients.

When considering these factors in relation to lack of hemisphere specific results in this thesis, it is possible that use of larger groups with a broad spectrum of abilities could have attenuated detection of possible group differences, an idea that has been suggested in previous studies (Gott 1973, St James Roberts 1981). As only three cases in this study have PIQ scores within the average range, one cannot draw reliable conclusions from these cases regarding laterality of function. It was of interest however to examine individual cases to determine whether results agreed with previous work examining small cohorts. It was particularly striking that there were no instances of prosopagnosia or visual hemineglect after right hemispherectomy, which supports previous arguments that suggest default engagement of damaged regions in situ prevents expression of compensatory abilities within the intact hemisphere (Plourde and Sperry 1984, de Gelder et al 1998). An important caveat is that there were no reports of prosopagnosia or neglect in patients with right hemisphere pathology pre-operatively, when the damaged hemisphere was in situ. It is acknowledged however that a detailed battery of assessments is often needed to unveil these deficits (Sergent and Villemure 1989), and therefore it is not unreasonable to speculate that possible difficulties with spatial attention and face recognition may have been present in some cases before surgery.

Kohn and Dennis (1974) proposed that visual cognitive function in the isolated left hemisphere did not mature beyond 10 years of age. There were several right hemispherectomised patients (**GB$_{R}$4, SN$_{R}$5, KD$_{R}$8, BC$_{R}$9, EBK$_{R}$10**) within this thesis that demonstrated levels of function above this level (Line bisection and sky search : chapter 4, Mooney closure of faces : chapter 5, Benton left-right orientation test, Money map : chapter 6, VMI and RCFT copy trial : chapter 7), though admittedly these achievements were not consistently evident across tasks for each patient. Nevertheless, these islands of skills reflect the capacity of the lone left hemisphere to develop a repertoire of visual cognitive skills that mature beyond the age of 10 years. The question remains as to why some skills appear to reach these levels of maturity and not others, and why different patterns of success and deficit occur across individuals. Use of a wider range of assessments to see if patterns emerge for different tasks, and further analysis including scores from language assessments to see if success and impairment on different tasks appear to correlate may help to illuminate factors contributing to the development of visual cognitive skills in the lone hemisphere.

Collectively, results reported in this thesis support the notion that in the context of brain injury sustained in childhood, the intact hemisphere is able to develop a repertoire of basic visual cognitive skills regardless of side of injury. This accords with the assertion that either hemisphere can mediate simple visual cognitive functions (Miosec 1993, Kohn and Dennis 1974, Ogden 1989 Banich 2000), which makes adaptive sense when one considers the necessity of being able to draw attention to salient events throughout the entire visual field. The establishment of a broad range of functions each with limited capacity would also enable input driven development to sculpt circuits that were most frequently employed in everyday life. This may involve altering a prespecified trajectory of hemispheric specialisation in order to acquire a basic armamarium of skills that are considered necessary such as basic spatial reference frames and processing salient visual stimuli such as familiar objects and faces. This would support theories of interactive specialisation (Johnson 2000), whereby development of lateralised functions are mitigated by brain injury as subsequent reorganisation must achieve a balance between quantity and quality of available functions within a finite amount of processing space.

The presence of global reduction of cognitive function in hemispherectomised patients contrasts with material specific deficits observed in studies of children with focal lesions (Stiles 1997, Vargha-Khadem 2001) or focal epilepsy (Helmstaedter and Lendt 2001). It remains possible that large or multifocal unilateral lesions leading to hemispherectomy may be of sufficient magnitude to obscure material specific impairments that may have been observed with smaller lesions. It is also difficult to disentangle the effects of large unilateral cerebral lesions from the presence of epilepsy as each have been shown to cause impairments of cognitive function independently of the other (Vargha-Khadem 1992, Muter et al 1997, Jokeit et al 2002). Severe generalised epilepsy may therefore be perceived as an unfortunate sequela that perpetuates and amplifies the damage caused by the original insult, hence obscuring any potential discrete impairments. It has also been argued that hemispheric differences emerge on more complex measures of visual cognitive function such as complex extrapersonal orientation (Kohn and Dennis 1974), processing of facial configuration (Le Grand 2003), mental rotation (Ogden 1989), and construction of spatially accurate drawings (Stiles 1997, Strauss and Verity 1983). This was not supported by results in this thesis. Whether general cognitive impairment or hemispheric equipotentiality attenuated such differences remains to be elucidated with larger samples of patients with age appropriate PIQ scores. Other factors that may have contributed to the pattern of observed results include 1) limitations of the types of assessments used in terms of isolating left and right hemisphere functions (Akshoomoff et al 2002), 2) use of heterogenous groups in terms of a) congenital vs acquired pathology and implications for reorganisation of function (Vargha-Khadem 1993), b) aetiology - Sturge-Weber syndrome has a predilection for occipito-parietal areas (Thomas-Sohl et al 2004) and bilateral damage is common with dysplastic lesions (Doring et al 1999), age at seizure onset, severity of seizure disorder and presence of seizure free periods and their impact on reorganisation of function (Elger et al 2004), c) pre-operative cognitive level of function and educational experience (Battaglia et al 1999), d) age at surgery (Sergent and Villemure 1989) and e) post surgical recovery periods (Milner 1975).

8.3 One versus two hemispheres

Comparison of hemispherectomised patients and matched controls was useful for several reasons. It enabled a general impression to be obtained of whether seizures principally affecting one hemisphere and damaging it extensively to the point of surgical removal affects visual cognitive function differently to having epilepsy currently affecting two hemispheres. It also enabled investigation of an important point raised by Bishop (1983), regarding attempts to separate the effects of generic reduction of cognitive function from effects of limited processing space. Comparison of hemispherectomised patients and controls matched for general intelligence levels would therefore permit investigation of possible limitations in cognising with one hemisphere that are above and beyond generic reduction of general cognitive function. This point bears on the third reason for comparing patients and controls, namely to address the concept of division of labour. Previous research suggests that complex tasks tend to be divided between the hemispheres in neurologically intact individuals (Green 1984, Lamb 1990, Banich and Belger 1990, Hellige 1993), which can also be applied to the fundamental distinction of language being lateralised to the left hemisphere and visuospatial functions residing in the right hemisphere. Absence of division of labour could be a potential explanation for impaired performance on complex visual cognitive tasks in hemispherectomy patients.

The rationale for selection of a control group was addressed in chapter two, and accords with previous studies advocating the use of a non surgical epilepsy control group for investigating cognitive outcome in patients that have undergone epilepsy surgery (Smith et al 2002). It is acknowledged that hemispherectomised patients and controls in this study are currently affected by different variables relevant to cognitive function. Functional variables such as ictal and interictal activity and anticonvulsant medication may potentially affect control participants (Elger et al 2004), whereas hemispherectomised patients cognise with the obvious morphological difference of an isolated hemisphere. The obvious common factor to both groups however, is that available neural substrates have been vulnerable to generalised seizure activity (Smith et al 2002). It was of interest that hemispherectomised patients and their controls demonstrated similar performance on most measures of visual cognition examined in this study. This suggests that when non-verbal intelligence scores are controlled for, visual cognitive function within a lone hemisphere that was exposed to seizure generalisation prior to surgical removal of its counterpart, is of similar integrity to cognising with two hemispheres that are currently affected by seizure activity. The fact that both hemispherectomised patients and controls demonstrate generally impaired performance across tasks reported in this thesis serves to illustrate the deleterious consequences of seizure activity in the developing brain (Vargha-Khadem et al 1992, Sillanpaa et al 1998, Hermann et al 2002, Motamedi and Meador 2003). Although hemispherectomised patients in this thesis are practically seizure free, the legacy of severe generalised seizure activity prior to surgery manifests as global reduction in cognitive function that cannot be solely attributed to lack of processing space. In turn, these findings provide more general support for Bishop's claim that apparently selective deficits in hemispherectomised patients on complex tasks are not a result of cognising with a lone left or right hemisphere per se, but manifest as a result of generic reduction of cognitive function. It seems that in the context of severe cognitive impairment there is no advantage to cognising with two hemispheres, which may imply that either 1) division of labour occurs less readily in the face of cognitive impairment as complex material cannot be processed effectively or 2) the products of division of labour are of limited sophistication due to cognitive impairment. These assertions are supported in this thesis by hemispherectomised patient and control groups both demonstrating intact performance on simple tasks and being impaired on more complex tasks.

The question remains whether hemispherectomised patients and controls without generalised cognitive impairments perform differently on tests of visual cognition. Due to a very small number of patients in this category in the current study, it was not deemed feasible to make the comparison to controls, though dissociation between general levels of intellectual function and performance on more detailed measurements of visual cognition has been alluded to in section 8.1. It makes intuitive sense that differences would be more likely as there would be more data from complex tasks that were not confounded by floor effects. Further study using a larger sample of patients with preserved PIQ and matched controls would be a valuable avenue of enquiry regarding the question of cognising with one versus two functional hemispheres.

The possibility of patients and controls demonstrating different levels of performance on complex tasks due to greater likelihood of division of labour receives partial support from this study. Statistically significant differences between patients and controls were evident on measures of complex visual search (chapter 4), perceptual discrimination of simple designs and memory for complex designs (chapter 7), suggesting that some limitations of visual cognitive function in the lone hemisphere may occur above and beyond those imposed by generalised cognitive impairment. This small collection of positive findings illustrates the problem of task complexity in revealing between groups differences. All groups were relatively adept at simple tasks, and impaired on more complex tasks, yet certain measures (Balloons test, Map mission, visual perception subtest of the VMI) may be of sufficient complexity to enable groups to fractionate into different levels of ability. The same argument could be proposed for detection of differences according to side of hemispheric removal, though task nature as opposed to complexity may relate more directly to hemispheric differences. It is also of note that each of these tasks require perceptual discrimination between multiple elements to detect a target within a specified time limit. Investigation of this domain using perceptual discrimination tasks that do not rely heavily on motor speed may represent an interesting avenue of further enquiry. The domain of visual memory was not directly assessed in this study due to time constraints. Suggestions regarding possible links between patient-control differences on tests involving perceptual discrimination and memory were alluded to in chapter 7 when considering the link between efficient stimulus registration and subsequent recall and recognition. Tentative evidence for group differences should be addressed in further studies by inclusion of a comprehensive battery of memory assessments to confirm or refute these findings.

8.4 Age at seizure onset and visual cognitive abilities

Teuber's (1975) concept of crowding out of visuospatial functions as a result of prioritising linguistic function after brain injury has been alluded to in previous hemispherectomy outcome studies (Ogden 1988, 1989, Mariotti 1998) whereby left hemispherectomy patients demonstrated better verbal than non verbal cognitive skills. The same concept has also been extended to the general finding of better verbal than performance IQ scores regardless of side of hemispheric removal (St James-Roberts 1981, Ogden 1989, 1996, Marriotti 1998, Battaglia 1999). It was therefore of interest to see whether the same phenomenon was generally evident in left hemispherectomised patients in the current study. When considering plasticity and reorganisation of function after brain injury, one must consider the interaction between timing of brain injury and plasticity of viable neural circuitry. It was predicted that early left hemisphere injury would enable language to develop and/or reorganise in the right hemisphere at the expense of visual cognitive skills as a result of prioritisation of linguistic function within limited processing space. This prediction also appeals to theories of ontogenetic and interactive specialisation (Vargha-Khadem 1992, Johnson 2000), which imply that hemispheric specialisations become established as development proceeds, hence early injury would be more likely to disrupt prespecified patterns of hemispheric specialisation as these patterns have yet to become fully established. Although the hemispherectomised patient group used in this study was larger than most groups in previous outcome studies, it was not deemed appropriate to perform analyses based on groups with congenital and acquired lesions due to unequal numbers of left and right hemispherectomy patients in each group. Grouping patients according to timing of brain lesions was also deemed unsuitable due to difficulties establishing precisely when brain lesions occurred during development. Age at seizure onset was therefore deemed the most suitable variable to test the prediction as it represents a physiological lesion that provides impetus for reorganisation of function, whose onset is relatively conspicuous and its deleterious effects on cognitive development are well documented.

When considering general levels of intelligence, findings in this study suggest that verbal-performance IQ discrepancies were usually in favour of the former, providing some support for the crowding hypothesis though it is acknowledged this was not supported by statistically significant findings from group comparisons. There were however significant positive correlations between age at seizure onset and performance IQ measures for the hemispherectomy group, lending further weight to the concept of crowding. Results from other investigations in this thesis were generally supportive of a positive association between age at seizure onset and visual cognitive function, though support was by no means complete, and it was not solely observed after left hemisphere injury, with positive associations being observed in right hemispherectomised patients and the control group on measures of visual attention suggesting a general advantage of late onset of seizures and visual cognitive function. Most studies documenting the effects of epilepsy tend to report associations between seizure onset and general levels of cognitive function, so it is difficult to reach direct conclusions regarding visual cognitive function specifically. The literature is complex but generally supportive of the notion that early onset of seizures is more detrimental to cognitive function than later onset of seizures (Elger et al 2004, Zaroff et al 2005, Mangano et al 2005 but see Thompson and Duncan 2005). Nevertheless, the vast majority of positive correlations between age at seizure onset and visual cognitive function were observed in the left hemispherectomy group, particularly on measures of face processing, spatial processing and measures of construction. These results support the concept of crowding and interactive specialisation in that later onset of seizures in the left hemisphere are less likely to have adverse effects on visual cognitive function in the lone right hemisphere, which accords with the notion of established hemispheric specialisation in the right hemisphere being less likely to be disrupted by left hemisphere injury as development proceeds. Further study using larger sample sizes to address potential differences between congenital versus acquired injuries could be informative. Patients with congenital injuries and/or early onset of seizures would be expected to have relatively intact language function compared to visual cognitive function regardless of side of hemispheric injury, whereas patients with acquired left hemisphere injuries and/or later onset of seizures would be expected to demonstrate the reverse profile with increasing age at onset of pathology/seizures. It must be acknowledged that consideration of the validity of the crowding hypothesis in this thesis is limited by assessments focusing solely on visual cognitive function, with no direct comparison to linguistic function. Future studies should compare visual cognitive and linguistic function in each patient to assess levels of sophistication achieved within different domains, to determine whether verbal and non-verbal functions have reached similar levels of maturity within the isolated hemisphere. Neuroimaging studies may also offer useful insight into the neural substrates employed for linguistic and visual cognitive functions within the lone hemisphere, enabling comparison of activation profiles with neurologically intact individuals. Previous studies have shown that linguistic function after left hemisphere injury is associated with increased activity in the right inferior frontal gyrus compared to neurologically intact controls (Voets et al 2005). The question remains as to the degree of overlap between activation profiles for verbal and non- verbal functions in the isolated hemisphere.

8.5 Future directions

Results from this comprehensive analysis of visual cognitive function after hemispherectomy has generated a thicket of interesting questions that demand further enquiry. Suggestions for future research based on assessments used have been included in each chapter with respect to modification of current tasks and will be briefly revisited here. These modifications would enable further confirmation and extension of current findings. Use of more controlled experimental paradigms such as restriction of head movement during midline stereopsis (chapter 3) would facilitate an attempt to confirm Hirai's (2002) findings of midline stereopsis in hemianopes. Recording of scanpaths and cancellation patterns in visual search tasks (chapter 4) would inform the debate regarding whether visual search in hemispherectomised patients is systematic or haphazard compared to control participants, and whether attentional effort is divided equally between the two visual hemifields. Face processing tasks (chapter 5) could be simplified e.g., using expression matching as opposed to naming in the Ekman faces task (Singh 2005), use of faces known to be familiar to each patient in the recognition task, and floor effects on the Jane task could be reduced by amplifying differences between faces on the configural and contour sets. Recording of movement sequences when drawing items made of multiple elements would be useful in order to investigate execution of graphic formulas (Stiles 1997) and their redescription when challenged with novel designs (chapter 7).

Visual cognition is a vast subject and examination of its entirety was beyond the scope of this thesis. Notable omissions from the testing protocol were investigation of object perception, visual memory and exploration of residual vision in the blind field otherwise known as "blindsight" (Weisktrantz 1996). Investigation of object perception in terms of discrimination and recognition from canonical and unusual views would provide an interesting comparison to the integrity of face processing in hemispherectomised patients and their controls, and may inform the debate surrounding the specialised role of the left hemisphere in object processing (de Renzi 2000). Use of a comprehensive battery of assessments designed to examine different aspects of visual memory would also be interesting and informative in light of the paucity of available literature focusing on this domain of function in hemispherectomised patients (Vargha-Khadem and Polkey 1992). As mentioned previously, comparison of performance in assessments of language and visual cognition in each patient could address the validity of the crowding hypothesis more completely, with the expectation that scores on language assessments would be better than scores on visual cognitive assessments in hemispherectomised patients with congenital and early acquired injury with early onset of seizures. This profile would be expected to reverse for hemispherectomised patients with left hemisphere insult acquired later in childhood or late onset of seizures. Use of fMRI and ERP techniques would enable comparison of activation profiles of hemispherectomised subjects, their age and PIQ matched controls and age matched neurologically intact individuals in an attempt to compare overlap between groups in terms of neural substrates involved in different aspects of cognitive function.

Another avenue of enquiry that was not directly addressed in this thesis is the possibility of residual vision in the blind hemifield otherwise known as blindsight. Although most of the available literature is dedicated to hemianopes with occipital lesions, previous studies have shown positive results in hemispherectomised patients in terms of detection of point light sources (Perenin and Jeannerod 1978, Ptito et al 1991), and summation across the vertical meridian (Tomaioulo et al 1997). These observations are of crucial importance regarding the debate surrounding the neural basis of blindsight, as these patients do not have islands of spared extrastriate cortex contralateral to the blind hemifield (Ptito 2001). Blindsight studies have been criticised for failing to consider eye movements and intraocular light scatter (King et al 1996, Stoerig et al 1996, Faubert et al 1999). Experiments using more reliable paradigms that address these confounds have still yielded positive results in hemispherectomised patients (Tomaioulo et al 1997), including evidence from an fMRI study reporting activation within striate and extrastriate regions of the intact hemisphere when stimuli were presented to the blind hemifield (Bittar et al 1999). Further study is needed to replicate previous findings in hemispherectomised patients, using paradigms that are amenable to individuals with cognitive impairment and limited concentration span. Marcel's (1997) replication of a flashgun method used by Torjussen (1976) is a good example of an experimental paradigm that requires minimal head and eye movement restraint, and responses consist of simple line drawings of stimuli that were observed as opposed to verbal description and confidence ratings.

8.6 Conclusion

In summary, the investigations described in this thesis have comprehensively documented patterns of impairment in visual cognitive function after hemispherectomy for intractable childhood epilepsy. The findings were broadly consistent with theories of equipotentiality and interactive specialisation, whereby the unfolding of a hemisphere specific architectural blueprint may be disrupted by cerebral injury. This enables a range of functions to develop in either hemisphere, albeit with limitations that may result from generic reduction in cognitive function, prioritisation of language skills, lack of processing space or subtle damage to regions that are critical for development of mature visual cognitive function. Use of a relatively large cohort revealed a broad spectrum of possible outcomes, consistent with previous studies. Correlations between age at seizure onset and task performance in the left hemispherectomised patients provided some support for the crowding hypothesis. Further study is needed to validate these findings and to chart new territory, using a detailed battery of neuropsychological and experimental tasks in conjunction with neuroimaging techniques.

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Appendix A. Recruitment letter for Hemispherectomised patients

Dear parent

For some years now, Professor Charles Polkey and our team at Great Ormond Street Hospital have been working together to study different aspects of cognitive ability such as language and movement in children and adolescents who have had brain surgery. The project has now developed a little further, and we are now planning to look at visual and spatial abilities. This involves abilities such as recognising faces, navigating through mazes and looking at details and outlines of visually presented material.

We have not yet had the pleasure of meeting you and [name], so we would be delighted to invite you to the Wolfson Centre, Institute of Child Health, to take part in this new project. It would be most ideal if you could come and visit us for the assessment sessions at some point over the next few months. We can arrange for these sessions to take place at a time that is best for you. Each of the assessment sessions will cover different activities. Firstly, we would ask [name] to complete some puzzles and pen and paper tasks. Secondly, we would ask [him/her] to take part in some tasks that examine how we recognise faces, to think about details and outlines of different pictures of objects and patterns, and to work through mazes. Some of these tasks may be familiar to [name] as part of assessments that have already taken place before the surgery. We have included information sheets with this letter that will give you and [name] more details of the study. There is also a questionnaire enclosed that relates to [name]'s visual ability in everyday life. If you decide not to participate in the study, it would still be very helpful to us if we could receive a completed questionnaire, although there is no obligation to do so.

If you would like more information about the study or would like to discuss your participation, we would be happy to call you on the telephone and answer any questions that you may have. After we have established telephone contact, we will then arrange a convenient time for you and [name] to visit us at the Wolfson Centre, Great Ormond Street Hospital for Children. All your travel costs will be refunded. If you have any questions about taking part in this study, please contact Rachel Thomasson either by telephone on 0207 905 2938 or by e-mail on R.thomasson@ich.ucl.ac.uk. Participation is voluntary and you are free to withdraw at any point from the research project. This will not affect any current or future treatment you may receive from Great Ormond Street Hospital. If you would like to be informed of the results of the study, or the individual results of your child, we are happy to provide this information. The results of this study should be very helpful to carers, teachers, and other professionals who are working with individuals with brain surgery.

If you would like to consider this further please complete the details on the slip below and return using the prepaid envelope. A member of our team will then contact you to discuss the research in more detail.

Appendix B1. Information for parents.

Information for Parents (male participants)

We would like to ask your permission to include [name] in this new research project.

1. **Title of project**

Visual perception and cognition after hemispherectomy.

2. **The aim of the study**

The aim of this study is to examine visual and spatial abilities after the surgical removal of a cerebral hemisphere, a procedure known as hemispherectomy. We also aim to increase our understanding of the different ways in which children take in visual information (perception) and understand it (cognition) after this type of operation. Visual and spatial abilities are very important in everyday life, and include skills such as seeing and remembering, picking out familiar objects, recognising them even though they have been changed in some way, and finding ones way around.

3. **Why is the study being done?**

The study will provide important information about the types of visual and spatial abilities that are spared after hemispherectomy, and those abilities which are affected. We will look for subtle impairments and remaining abilities that may not have been examined closely in routine assessments. This study may be able to contribute to future research that will focus on the development of more detailed assessment schemes for visual and spatial abilities. It may also provide valuable information for rehabilitation programmes that focus on making the best possible use of abilities which have been spared, and improving those that have been affected.

4. **How is the study to be done?**

We will begin by asking you and [name] questions about his progress before and after the operation, the time course of the epilepsy, and details of any medication currently being taken. This information is put together as a developmental history, and provides us with important background information. We would then take a measurement of his field of vision and visual acuity. This will give us an impression of how small or large the blind field of vision is, and how well he can see small details.

After this we would arrange three assessment sessions, each lasting for one morning or afternoon. These assessment sessions can either take place over one and a half days, or one day and another half day at some other point, depending on what is best for you and [name].

Sessions 1-2: The first two assessment sessions will involve several tasks involving puzzles, looking at faces, shapes and pictures and drawing tasks. The tasks are standardised, which means they provide us with a reliable estimate of ability for a particular age group. Many of the tasks can be fun, and each takes between 5 minutes and 30 minutes. Each testing session will last approximately 2.5 to 3 hours, including breaks. We will always tell [name] what the tasks involve and why we are doing them. A research student working under the direction of Professor Vargha-Khadem will work with him during these tasks.

Session 3: In this session, [name] will be asked to carry out tasks that will examine his ability to recognise faces and pick out details in faces. This will involve seeing human, animal and cartoon faces on a computer screen or as photographs. Some of the faces will be familiar, others will not be familiar. He will be asked questions about the faces such as "are they pictures of the same person?" "is it a man or a woman?" The appearance of the faces may be altered in some way, or they may be shown upside down. He will also be asked to complete a series of tasks that examine spatial ability. Examples include finding the way through mazes, picking out a shape from a collection that he has seen before, remembering location of shapes and objects, and concentrating on details and outlines of visual stimuli. These tasks will be a combination of pencil and paper type tasks and computerised tasks.

Additionally, we may wish to carry out some studies looking at the pattern of brain activity that occurs during a particular task. In one type of study, small sensors would be placed on [name]'s head to record the electrical activity of his brain. During the recording, he would be asked to do some of the tasks he had encountered previously in earlier sessions. These are painless procedures. The recording time should last approximately 30 minutes including breaks.

If you wish, we can help you arrange transport and/or accommodation for your visits to us. We will arrange the assessment days with you to be at times that are most convenient for you and [name].

5. Are there risks and discomforts?
The testing sessions can sometimes feel lengthy, most of them lasting between 1-2 hours, although there are frequent breaks throughout the testing sessions if needed.

6. What are the potential benefits?
This research project may not bring any immediate benefits to [name]. However, we hope that in due course the information we obtain from this research project will help childrens educational development and quality of life through the development of more detailed assessment procedures and rehabilitation programmes for children and adolescents who have had brain surgery.

7. Who will have access to the case/research records?
Access to the case/research records will be available to the collaborators working on the research project and to a representative of the Ethics Committee.

8. Does my son have to take part in the study?
No. If you or [name] decide now or at a later stage that you do not wish for him to participate in this research project, that is entirely your right and will not in any way prejudice any present or future treatment.

9. Will I be paid for taking part in this study?

We will refund all your travel and accommodation expenses. In addition, as a small token of our appreciation, we will also give [name] a book/record token, or a ticket to see one of the many attractions in London such as the London eye.

10. Who do I speak to if problems arise?

If you have any complaints about the way in which this research project has been or is being carried out, please in the first instance, discuss them with the researcher. If the problems are not resolved, or you wish to comment in any other way, please contact the Chairman of the Research Ethics Committee, by post via the Research and Development Office, Institute of Child Health, 30 Guildford street, London WC1N 1EH, or if urgent, by telephone on (020) 7242 9789 ext. 2620 and the Committee administration will put you in contact with him.

Researcher who will have contact with the family:

Professor Faraneh Vargha-Khadem and Rachel Thomasson.

Details of how to contact the researcher

Appendix B2 Information for participants

We would like to ask you if you want to take part in this new research project.

11. **Title of project**
Visual perception and cognition after hemispherectomy. This means how we see things (perception), and how we think about things we have seen (cognition). For instance, if you see a cat, you will take notice of how big it is, what colour it is, whether it is sitting still or moving. Seeing colours, sizes and shapes are what we call perceptions. Once you have a picture of the cat in your head, you might compare it to other cats you have seen to see if you have met it before, or store the picture away so you can remember it later. The skills we use to do these types of things are called cognitions.

12. The aim of the study
We aim to understand more about the different ways in which children take in visual information (perception) and understand it (cognition) after a type of brain operation known as hemispherectomy. This involves removing a cerebral hemisphere of the brain. Visual and spatial skills are very important in everyday life, and include things such as seeing and remembering, picking out things we have seen before from those we have never seen before, recognising them even though they have been changed in some way, and finding ones way around.

13. Why is the study being done?
The study will give us important information about the types of visual and spatial skills that are still okay after this operation, and those skills which have been affected. We will look at the types of skills that may not have been tested in ordinary hospital appointments. This study may be able to help future research that will try to develop more detailed tests for visual and spatial skills. It may also be helpful for people working in hospitals that try to make the best possible use of skills which are still okay, and improving those skills that have been affected.

14. How is the study to be done?
Firstly we would ask you some questions about how you have been getting along, and what your epilepsy is like. We would then measure your field of vision and visual acuity. This will tell us how small or large your blind field of vision is, and how well you can see small details. After this we would arrange three assessment sessions, each lasts for one morning or afternoon. These assessment sessions would take place over a day and a half or one day and another half day at some point depending on what is best for you. The first two assessment sessions will have a collection of tasks involving puzzles, looking at faces, shapes and pictures and drawing tasks. Many of the tasks can be fun, and each takes between 5 minutes and 30 minutes. Each testing session will last about 2.5 to 3 hours, including breaks. We will always tell you what the tasks are about and why we are doing them. A research student working under the instruction of Professor Vargha-Khadem will work with you during these tasks.

In the third session, you will be asked to carry out tasks that will look at how you recognise faces and pick out details in faces. You will see human, animal and cartoon faces on a computer screen or as photographs. Some of the faces will be familiar, others will not be familiar. We will ask you questions about the faces such as "are they pictures

of the same person?" "is it a man or a woman?" The appearance of the faces may be altered in some way, or they may be shown upside down.
We will also ask you to complete some tasks that examine spatial ability (how we see and remember where different things are, where things are in relation to where we are). Examples include navigation through mazes, picking out a shape from a collection that you have seen before, remembering where shapes and objects are, and concentrating on details and outlines of things. These tasks will be a combination of pencil and paper type tasks and computerised tasks.

Additionally, we may want to do some studies looking at the pattern of brain activity that happens as you do a certain task. In one type of study, small sensors would be placed on your head to record the electrical activity of your brain. During the recording, you would be asked to do some of the tasks you have done before. This sort of study takes around 30 minutes including breaks.

If you wish, we can help you arrange transport and/or accommodation for your visits to us. We will arrange the assessment days with you to be at times that are best for you.

15. Are there risks and discomforts?
The testing sessions can sometimes feel lengthy; most of them lasting between 1-2 hours, although there are frequent breaks throughout the testing sessions if needed.

16. What are the potential benefits?
This research project may not bring any benefits to you straight away. However, we hope that in the future, the information we collect from this research project will help children to do better at school and at home. We can help to do this by giving our information to other researchers who are trying to design more detailed tests of visual skills and improving skills of children and adolescents who have had brain surgery.

17. Who will have access to the case/research records?
Access to the case/research records will be available to the people working on the research project and to a representative of the Ethics Committee.

18. Do I have to take part in the study?
No. If you or you decide now or at a later stage that you do not want to take part in this research project, that is entirely up to you.

19. Will I be paid for taking part in this study?
We will refund all your travel and accommodation expenses. In addition, as a small token of our appreciation, we will also give you a book/record token, or a ticket to see one of the many attractions in London such as the London eye.

20. Who do I speak to if problems arise?
If you are not happy about the way in which this research project has been or is being carried out, please talk about it with the researcher. If the problems are not solved, or you wish to tell someone else, please contact the Chairman of the Research Ethics Committee, by post at the Research and Development Office, Institute of Child Health, 30 Guildford

street, London WC1N 1EH, or if urgent, by telephone on (020) 7242 9789 ext. 2620 and the Committee administration will put you in contact with him.

Researcher who will have contact with the family:
Professor Faraneh Vargha-Khadem and Rachel Thomasson.

Details of how to contact the researcher
Contact Rachel Thomasson at:

Appendix C - vision questionnaire for hemispherectomised patients (questions relating to surgery were omitted for controls)

Vision Questionnaire

This questionnaire will provide important information for the study, and may be completed by a relative, a close friend, and/or   himself. Please fill in the details as best you can. If you have decided not to participate in the assessment sessions at the Wolfson centre it would still be a great help to receive a completed questionnaire.

If you are a relative or a friend, please indicate your relationship to ____________

1. Date of birth: ____________________ (Please tick the correct boxes)

2. Is he left or right handed?...Left ☐ Right ☐

3.Was he left or right handed before the hemispherectomy?...................... Left ☐ Right ☐

4a)Approximately how old was he when the seizures began?____________________

4b)Approximately how old was he when the hemispherectomy was performed? __________

5.Was it a Left or right sided hemispherectomy?.............................Left ☐ Right ☐

6.Were there any visual problems before surgery?

a) Blindness in part of the visual field.. Yes ☐ No ☐

b) Shortsightedness.. Yes ☐ No ☐

c) Longsightedness.. Yes ☐ No ☐

d) Squint.. Yes ☐ No ☐

e) Eyes darting back and forth -difficulty maintaining focus on things.......Yes ☐ No ☐

f) Dislike of bright light ....Yes ,often ☐ Yes, occasionally ☐ No ☐

g) Blurring of vision......................Yes ,often ☐ Yes, occasionally ☐ No ☐

h) Tunnel vision......................Yes ,often ☐ Yes, occasionally ☐ No ☐

i) Problems telling different colours apart...Yes ,often ☐ Yes, occasionally ☐ No ☐

j) Problems telling different shades

of the same colour...................... Yes ,often ☐ Yes, occasionally ☐ No ☐

k) Difficulties seeing in the dark......................Yes ,often ☐ Yes, occasionally ☐ No ☐

Other (please describe as best you can)______________________________

7a)If yes to any of the above, at what age were they noticed?____________________

7b)Did any of the above coincide with onset of seizures?____________________

8. Does he wear glasses?.. Yes ☐ No ☐

If yes at what age did he begin wearing them? __________

9. Is he able to see in the dark?......................Yes, quite well ☐ Yes, a little ☐ No ☐

10. Is he able to tell which parts of something are darker and

lighter e.g the darker and lighter bits of a black and white photo?..............Yes ☐ No ☐

12. Is there any difficulty recognising different colours?

E.g. blue and green, red and orange .... Yes, often ☐ Yes, occasionally ☐ No ☐

13. Is there any difficult recognising

different shades of colours?..Yes, often ☐ Yes, occasionally ☐ No ☐

14. Does he orient towards visual stimuli? ....Yes, often ☐ Yes, occasionally ☐ No ☐

15. Does he actively examine

his visual environment?..Yes, often ☐ Yes, occasionally ☐ No ☐

16. Does he reach and grasp for objects?...................Yes, often ☐ Yes, occasionally ☐ No ☐

17. What type of things does he tend to reach and grasp for?____

18. approximately what distance are things most clearly seen and recognised?____________

19. Is he aware of himself in the mirror?..Yes ☐ No ☐

20. Is there an eye or head position that seems to work best for your child with respect to visual ability?.........Yes ☐ No ☐ If yes please describe it briefly: _______________

____

21. Is his direction of gaze:

a)fixed in the middle? ....Yes ☐ No ☐

b)more to one side?..to the left ☐ to the right ☐

c)Able to move freely, following items of interest as they move? ....Yes ☐ No ☐

d)Moving randomly, seems unrelated to events in the visual environment ?...Yes ☐ No ☐

22. Is he able to stay focused

on an object of interest? .... Yes, often ☐ Yes, occasionally ☐ No ☐

23. Is he able to follow a moving object

with his eyes?.. Yes, often ☐ Yes, occasionally ☐ No ☐

24. Is he able to follow a moving person

with his eyes?... ....Yes, often ☐ Yes, occasionally ☐ No ☐

25. Does he follow your movements round the room with his eyes when you have given him no sound clues?...Yes, often ☐ Yes, occasionally ☐ No ☐

26. Will his eyes follow your direction of gaze

to see what you are looking at? ....Yes, often Yes, occasionally No

27. Can he tell if something is:

a)coming towards him?..Yes, often ☐ Yes, occasionally ☐ No ☐

b)moving away from him?..Yes, often ☐ Yes, occasionally ☐ No ☐

c)moving to the left of him?...Yes, often ☐ Yes, occasionally ☐ No ☐

d)moving to the right of him?.. Yes, often ☐ Yes, occasionally ☐ No ☐

28. Is he able to tell if something is moving

quickly or slowly? ....Yes, often ☐ Yes, occasionally ☐ No ☐

29. Does he tend to bump into people or objects,

a)in front of him?...Yes, often ☐ Yes, occasionally ☐ No ☐

b)Behind him?.. Yes, often ☐ Yes, occasionally ☐ No ☐

c)either side of him?..Yes, often ☐ Yes, occasionally ☐ No ☐

d)Above him? ....Yes, often ☐ Yes, occasionally ☐ No ☐

e)Things on the floor?..Yes, often ☐ Yes, occasionally ☐ No ☐

30. Does he respond to things in the blind part

of his visual field? ....Yes, often ☐ Yes, occasionally ☐ No ☐

31. Have you ever noticed him orienting towards something in his blind field of vision that was visual in nature without any sound clues?............Yes, often ☐ Yes, occasionally ☐ No ☐

32. Can he tell left from right? .... Yes ☐ No ☐

33. Can he tell where North, south, east, and west are?.. Yes ☐ No ☐

34. Is he able to estimate distance between himself and something

further away? E.g I am "about this much" away from the chair......................... Yes ☐ No ☐

35. Is he able to estimate distance between two things?

e.g the biscuit is "about this much" away from the box... Yes ☐ No ☐

36. Does he tend to describe where things are in relation

to each other - (e.g the biscuit is on top of the box,

the car is next to the house, the ball is behind the box)? ....Yes ☐ No ☐

37. Does he tend to be able to find his way around the house ?........................Yes ☐ No ☐

38. Does he tend to forget where things are kept in the house?.................... Yes ☐ No ☐

39. Does he tend to look for them in

the wrong places?...Yes, often ☐ yes, occasionally ☐ No ☐

40. Does he tend to be able to find his way around the local environment?........ Yes ☐ No ☐

41. Is he able to follow directions? ....Yes ☐ No ☐

42. Does he tend to get lost or turn in the wrong direction on a journey, a walk or in a building where he has often been before?.......Yes, often ☐ yes, occasionally ☐ No ☐

43. Is he familiar with any type of map? ....Yes ☐ No ☐

If so does he tend to point things out on the map? ....Yes ☐ No ☐

44. Does he use any maps or sets of directions to get from one place to another?....... Yes ☐ No ☐

45. Has he ever had a go at working through a maze in a puzzle book? ....Yes ☐ No ☐

46. Does he have some knowledge of shape and geometry?

a) Recognise different shapes? ....Yes ☐ No ☐

b) Comment on why they are different?....... Yes ☐ No ☐

c) Recognise different examples of shapes in the same category? ....Yes ☐ No ☐

d) Able to tell if something is symmetrical?....... Yes ☐ No ☐

47. Does he tend to

a) Wash on only one side?.......Yes, often ☐ yes, occasionally ☐ No ☐

b) Ignore food on one side of plate? .... Yes, often ☐ yes, occasionally ☐ No ☐

c) Leave out, distort, or put part of an object in the wrong place if drawing or copying?...... Yes, often ☐ yes, occasionally ☐ No ☐

48. Have you noticed any difficulty with naming or recognising objects? ....Yes, most ☐ Yes, some ☐ No ☐

If yes can you give one or two examples?______________________________

49. Are there any classes of object he is particularly good at naming and or recognising? ....Yes, most ☐ Yes, some ☐ No ☐

If yes can you give one or two examples?______________________________

50. Does he tend to recognise familiar objects e.g those around the house? ....Yes, most ☐ Yes, some ☐ No ☐

51. Does he recognise his own possessions ? ....Yes, most ☐ Yes, some ☐ No ☐

52. Does he recognise his own handwriting?.......Yes ☐ No ☐

53. Does he have any difficulty recognising, by sight, close relatives or friends that he meets frequently?

a) Close up? ....Yes, often ☐ yes, occasionally ☐ No ☐

b) Across the room?.......Yes, often ☐ yes, occasionally ☐ No ☐

☐ ☐

c) Across a road? ....Yes, often ☐ yes, occasionally No

54. Does he tend to recognise familiar faces in photographs? ....Yes, often ☐ yes, occasionally ☐ No ☐

55. Does he recognise different photographs of the same person?.. Yes, often ☐ yes, occasionally ☐ No ☐

56. Does he recognise key features of faces? (nose, eyes etc)............................Yes ☐ No ☐

57. Does he return a silent smile or imitate a face you pull?................................Yes ☐ No ☐

58. Does he have any difficulty recognising different facial expressions? ....Yes ☐ No ☐

59. Does he respond to your silent facial expressions?... Yes ☐ No ☐

60. Does he have any difficulty telling the difference between

a) Male and female faces? ....Yes, often ☐ yes, occasionally ☐ No ☐

b) Old and young faces? ....Yes, often ☐ yes, occasionally ☐ No ☐

61. Does he find that faces of famous people seen on television or in photographs look unfamiliar? ....Yes ☐ No ☐

62. Does he tend to recognise familiar faces in magazines?....................... ....Yes ☐ No ☐

63. Does he tend to recognise familiar cartoon faces in comics?...................... Yes ☐ No ☐

64. Have you noticed any difficulty with naming or recognising famous or familiar Buildings? .... Yes ☐ No ☐

65. Have you noticed any difficulty with naming or recognising famous or familiar scenery?.. Yes ☐ No ☐

66. Does he tend to recognise key features of scenes e.g sky, trees, clouds etc ?.. Yes ☐ No ☐

67. Does he tend to recognise key features of buildings e.g doors, windows, chimney etc?... ....Yes ☐ No ☐

68. Have you noticed him using his eyes to look through a collection of things to pick out what he wants before reaching for it? ....Yes ☐ No ☐

69. Can he pick out a small object by sight without having to feel for it first? ....Yes ☐ No ☐

70. Does he play any games that involve putting parts together to make a whole? .... Yes ☐ No ☐

71. Can he pick out parts of a whole,

e.g a nose in a face, a window in a house?.. Yes ☐ No ☐

72. Is he able to pick out different examples of the same category e.g different pairs of shoes, different jumpers, different dolls? ...Yes, generally ☐ Yes, sometimes ☐ No ☐

73. What types of games does he like to play?________________________________

74. Does he have any favourite story books? ________________________________

75. Does he enjoy seeing the illustrations in the story book?.. ...Yes ,often ☐ yes, sometimes ☐ No ☐

76. Does he like to read them himself or do you read them to him?...Reads himself ☐ Books are read to him ☐

77. Does he enjoy drawing? ....Yes, often ☐ Yes, occasionally ☐ No ☐

78. Are there certain things he likes to draw? ________________________________

79. Does he tend to copy things or draw from memory?.........Copy ☐ Draw from memory ☐

80. What are his favourite Television shows? ________________________________

81. What are his favourite Films? ________________________________

82. What are his favourite Cartoons? ________________________________

83. Does he have any favourite actors or actresses?________________________________

84. Does he have any favourite cartoon characters?________________________________

85. Does he have any favourite colours?________________________________

86. Does he have any favourite animals?________________________________

87. Does he recognise different animal noises?..Yes ,generally ☐ Yes, sometimes ☐ No ☐

88. Does he recognise different environmental noises such as rainfall, wind,? ....Yes, generally ☐ Yes, sometimes ☐ No ☐

89. Does he describe things from memory? ....Yes, generally ☐ Yes, sometimes ☐ No ☐

90. Does he ever describe images or scenes from dreams? ....Yes ,often ☐ Yes, sometimes ☐ No ☐

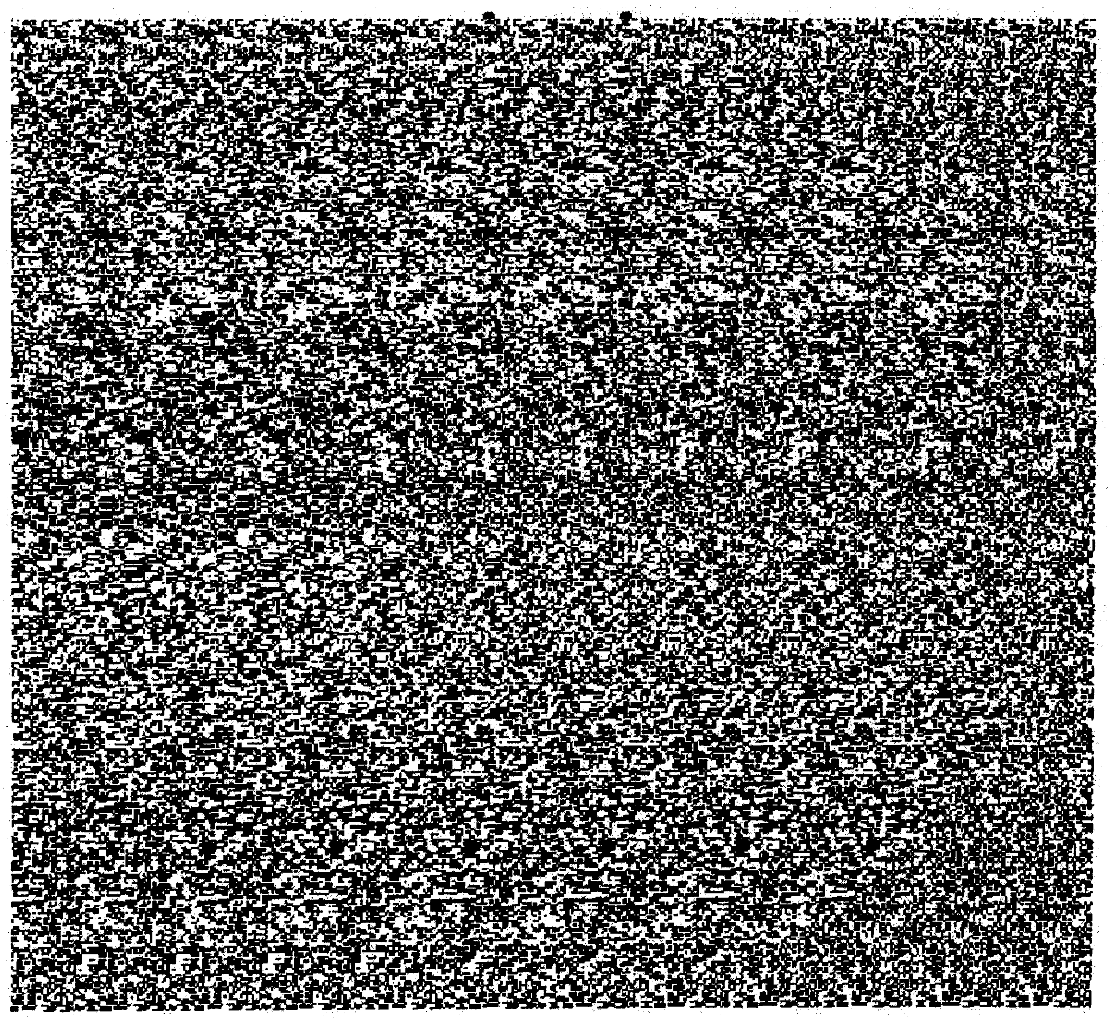
Thankyou very much for your time and patience

Appendix D. Breakdown of testing phases one and two

Phase One (two days)	Phase Two (one day)
Colour Blindness screen	Rey Complex figure test
Wechsler Scales	Jane task – upright sets
Benton Judgement of Line orientation	Axis 1 test
Visual object and space perception battery	Ekman faces
Stereopsis tests	Global and local processing test
Mooney closure faces test	Jane – inverted sets
Line Bisection test	
Semmes test of left-right discrimination	Categorical and metric processing test
Sky search	Famous faces
Mooney closure faces test	Axis 3 test
Star cancellation	PAGIT
Benton test of left-right discrimination	Shapes challenge test
Key search	
Money Road map Test	
Thurstone Closure Test	
Test of Visuomotor Integration	
Mazes	
Mental reorientation test	
Balloons Test	
Arrows	
Flags Test	
Map mission	

Appendix E : The random dot stereogram

The random dot stereogram (Julesz 1960) consists of a picture in which two images of a hidden figure have been superimposed and printed as a composite image. The images represent two retinal views of a three dimensional scene, and will evoke the perception of an image in depth when registered by each eye separately upon perception of binocular disparity cues. Monocular form perception cannot operate as no single retinal image provides sufficient figure-ground information. This becomes evident when closing one eye; the hidden figure disappears, only to reappear again when both eyes are open.



Chapter	Test	Left vs Right	Patient vs Control	Age at seizure onset
Two - baseline assessments	Wechsler Intelligence Scales			Age at seizure onset correlated with PIQ for left and right hemispherectomy patients.
Three - stereopsis	Titmus and TNO		All controls demonstrate stereopsis on both tests. Only 7 patients demonstrate stereopsis on both tests.	
Four - visual attention	Balloons subtest B		Controls outperform patients (total score)	Age at seizure onset correlated with Balloons B task (left controls)
	Sky search			Age at seizure onset correlated with total score (right controls)
	Map mission		Controls outperform patients (total score)	
Five - face processing	PAGIT, Jane task			Age at seizure onset correlated with scores on these tasks (left hemispherectomy)
Six - spatial processing	Semmes Body orientation			Age at seizure onset correlated with score on Semmes subset A (left and right hemispherectomy)
	Mental reorientation			Age at seizure onset correlated with total score (left hemispherectomy)
	Money road map			Age at seizure onset correlated with total score (left control)
	Axis 1 task			Age at seizure onset correlated with total score (left hemispherectomy)
	Axis 3 task			Age at seizure onset correlated with total score (left hemispherectomy)
	VOSP – number location			Age at seizure onset correlated with total score (left hemispherectomy)
	Spot the dot - metric			Age at seizure onset correlated with total score (left hemispherectomy)
Seven - construction	Test of Visuomotor Integration		Controls outperform patients on Visual perception subtest (total score)	Age at seizure onset correlated with most test scores in this chapter (left hemispherectomy).
	Rey Complex Figure	Recognition and cluster *inclusion* in delayed recall	Controls outperformed patients in cluster *placement* on immediate and delayed recall trials (total scores).	

APPENDIX F Summary table of significant results.